

EXHIBIT B4

April Zambelli-Weiner, Ph.D.

Page 210

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

-----x

IN RE JOHNSON & JOHNSON) MDL No.
TALCUM POWDER PRODUCTS) 16-2738 (FLW)(LHG)
MARKETING SALES PRACTICES,)
AND PRODUCTS LIABILITY)
LITIGATION)
THIS DOCUMENT RELATES TO)
ALL CASES)

-----x

V O L U M E I I

VIDEOTAPED DEPOSITION OF
APRIL ZAMBELLI-WEINER, Ph.D.
WASHINGTON, D.C.
THURSDAY, FEBRUARY 7, 2019
9:54 A.M.

Pages: 210 - 455

Reported by: Leslie A. Todd

April Zambelli-Weiner, Ph.D.

| Page 211 | Page 213 |
|--|--|
| <p>1 Deposition of APRIL ZAMBELLI-WEINER, Ph.D., 2 held at the offices of: 3 4 5 ASHCRAFT & GEREL, LLP 6 1825 K Street, N.W. 7 Washington, DC 20005 8 9 10 Pursuant to notice, before Leslie Anne Todd, 11 Court Reporter and Notary Public in and for the 12 District of Columbia, who officiated in 13 administering the oath to the witness. 14 15 16 17 18 19 20 21 22 23 24 25</p> | <p>1 APPEARANCES (Continued): 2 3 GEOFFREY M. WYATT, ESQUIRE 4 SKADDEN, ARPS, SLATE, MEAGHER & FLOM, LLP 5 1440 New York Avenue, N.W. 6 Washington, D.C. 20005 7 (202) 371-7008 8 9 ON BEHALF OF THE PCPC: 10 THOMAS LOCKE, ESQUIRE 11 SEYFARTH SHAW LLP 12 975 F Street, NW 13 Washington, D.C. 20004 14 (202) 463-2400 15 16 ON BEHALF OF THE IMERYS DEFENDANTS: 17 MICHAEL R. KLATT, ESQUIRE 18 GORDON & REES SCULLY MANSUKHANI, LLP 19 816 Congress Avenue 20 Suite 1510 21 Austin, Texas 78701 22 (512) 582-6485 23 24 25</p> |
| <p>1 APPEARANCES 2 3 ON BEHALF OF THE PLAINTIFFS: 4 CHRISTOPHER V. TISI, ESQUIRE 5 LEVIN PAPANTONIO, LLP 6 316 South Baylen Street 7 Pensacola, Florida 32502 8 (850) 435-7184 9 10 MICHELLE A. PARFITT, ESQUIRE 11 ASHCRAFT & GEREL, LLP 12 4900 Seminary Road, Suite 650 13 Alexandria, Virginia 22311 14 (703) 997-1774 15 16 ON BEHALF OF THE JOHNSON & JOHNSON DEFENDANTS: 17 MARK HEGARTY, ESQUIRE 18 SHOOK, HARDY & BACON, LLP 19 2555 Grand Boulevard 20 Kansas City, Missouri 64108 21 (816) 474-6550 22 23 24 25</p> | <p>1 APPEARANCES (Continued): 2 3 ON BEHALF OF PTI: 4 MICHAEL ANDERTON, ESQUIRE 5 TUCKER ELLIS, LLP 6 950 Main Avenue 7 Suite 1100 8 Cleveland, Ohio 44113-7213 9 (216) 696-4835 10 11 ALSO PRESENT: 12 DANIEL HOLMSTOCK (Videographer) 13 14 15 16 17 18 19 20 21 22 23 24 25</p> |

2 (Pages 211 to 214)

April Zambelli-Weiner, Ph.D.

| | Page 215 | | Page 217 |
|----|--|----|--|
| 1 | CONTENTS | | |
| 2 | EXAMINATION OF APRIL ZAMBELLI-WEINER, Ph.D. PAGE | | |
| 3 | By Mr. Hegarty 218, 441 | | |
| 4 | By Mr. Klatt 418, 449 | | |
| 5 | By Mr. Locke 426 | | |
| 6 | By Mr. Tisi 438, 446 | | |
| 7 | | | |
| 8 | E X H I B I T S | 8 | |
| 9 | (Attached to transcript) | 9 | |
| 10 | ZAMBELLI-WEINER DEPOSITION EXHIBITS PAGE | 10 | |
| 11 | No. 13 Cancer Prevention Coalition paper: | 11 | |
| 12 | Petition Seeking a Cancer Warning | 12 | |
| 13 | on Cosmetic Talc Products 221 | 13 | |
| 14 | No. 14 Excerpt from deposition of Linda | 14 | |
| 15 | Loretz, Ph.D 230 | 15 | |
| 16 | No. 15 Article entitled "Perineal talc use | 16 | |
| 17 | and ovarian cancer risk: A case | 17 | |
| 18 | study of scientific standards in | 18 | |
| 19 | environmental epidemiology" 234 | 19 | |
| 20 | No. 16 Article entitled "Perineal | 20 | |
| 21 | Application of Cosmetic Talc and | 21 | |
| 22 | Risk of Invasive Epithelial | 22 | |
| 23 | Ovarian Cancer: A Meta-analysis of | 23 | |
| 24 | 11,933 Subjects from Sixteen | 24 | |
| 25 | Observational Studies" 237 | 25 | |
| | | | |
| | Page 216 | | Page 218 |
| 1 | E X H I B I T S (Continued) | 1 | PROCEEDINGS |
| 2 | (Attached to transcript) | 2 | ----- |
| 3 | ZAMBELLI-WEINER DEPOSITION EXHIBITS PAGE | 3 | THE VIDEOGRAPHER: The time is 9:54 |
| 4 | No. 17 Article entitled "Factors Related | 4 | a.m., February 7, 2019. We are on the record with |
| 5 | to Inflammation of the Ovarian | 5 | video 1 of Volume II. |
| 6 | Epithelium and Risk of Ovarian | 6 | Unless you want the witness resworn. |
| 7 | Cancer" 277 | 7 | MR. HEGARTY: No, we're fine. |
| 8 | No. 18 Article entitled "Use of cosmetic | 8 | RESUMED DIRECT EXAMINATION |
| 9 | talc on contraceptive diaphragms | 9 | BY MR. HEGARTY: |
| 10 | and risk of ovarian cancer: a | 10 | Q Good morning, Doctor. |
| 11 | meta-analysis of nine observational | 11 | A Good morning. |
| 12 | studies" 325 | 12 | Q We're here for the continuation of your |
| 13 | No. 19 Article entitled "Perineal Talc | 13 | January 11th deposition. What did you do to |
| 14 | Use and Ovarian Cancer, A | 14 | prepare for this continued deposition? |
| 15 | Systematic Review and Meta-Analysis" 334 | 15 | A Sure. I went back over my report. I |
| 16 | No. 20 Power-Point slides 336 | 16 | went back over some of the underlying studies that |
| 17 | No. 21 Letter from PCPC to FDA, dated | 17 | I reference in my report. I read my depo |
| 18 | July 21, 2009 344 | 18 | transcript from the first session. And I may have |
| 19 | No. 22 Article entitled "Perineal Talc | 19 | looked at a few other documents. Like I recall |
| 20 | Exposure and Risk of Ovarian | 20 | looking at the IARC report on -- on talc. |
| 21 | Carcinoma" 345 | 21 | Q Do you recall any other specific |
| 22 | No. 23 Article entitled "Characteristics of | 22 | documents besides those you mentioned? |
| 23 | Women Who Use Perineal Powders" 369 | 23 | A No, not that I recall. |
| 24 | No. 24 Binder (retained by witness) 441 | 24 | Q Did you meet with any attorneys for |
| 25 | | 25 | plaintiffs to prepare for the deposition? |

3 (Pages 215 to 218)

Golkow Litigation Services - 1.877.370.DEPS

April Zambelli-Weiner, Ph.D.

| Page 219 | Page 221 |
|---|--|
| <p>1 A I met with Chris yesterday. 2 Q How long did you meet with Chris? 3 A Maybe like an hour and a half. 4 Q Was that the extent of the meetings you 5 had with counsel for plaintiffs since your last 6 deposition on the 11th? 7 A Yes. I believe so. 8 Q Have you communicated since your last 9 deposition with anyone outside of the litigation 10 regarding your report or your opinions in your 11 report? 12 A No, I don't think so. 13 Q Have you prepared any additional 14 invoices from those we marked when we were here 15 the last time for -- that -- that recorded your 16 work in this case? 17 A I don't believe so. 18 Q Do you recall -- or are you able to 19 estimate how much additional work you have done in 20 this matter since January 11th by hours? 21 A I can estimate for you. Maybe 16 hours, 22 20 hours. Something in that range. 23 Q Do you have your report in this case 24 that we had previously marked as Exhibit No. 8? 25 A Yes, I do.</p> | <p>1 Q You -- the first heading you have under 2 there is the 2008 Citizens Petition to the FDA. 3 First of all, do you understand that 4 it's "Citizen Petition" and not "Citizens 5 Petition"? 6 A I don't know for certain, but I'll take 7 your -- I'll take your word for it. 8 Q You talk about the Citizen Petitions 9 that were filed and you make reference to Samuel 10 Epstein. Did you do any research into who Samuel 11 Epstein is? 12 A I don't recall doing any research other 13 than perhaps looking him up at the time in terms 14 of his position with the organization that 15 submitted the petition. 16 Q Did you do any research about his 17 organization, the Cancer Prevention Coalition? 18 A No, I didn't. Not that I recall. 19 Q I'm going to hand you what I'm marking 20 as Exhibit 13, which is the 2008 Citizen Petition. 21 (Exhibit No. 13 was marked for 22 identification.) 23 BY MR. HEGARTY: 24 Q And you're familiar with this document, 25 correct?</p> |
| <p style="text-align: center;">Page 220</p> <p>1 Q We're going to be working from that 2 report really for the rest of the deposition. 3 A Okay. 4 MR. TISI: And, Counsel, I just want to 5 remind you that I -- that we did prepare that 6 binder that you -- a copy of the binder from -- 7 that we marked last time, and then another binder 8 with the studies that -- for ease of reference 9 that would correspond with the -- the charts that 10 she developed in her report. So I just wanted to 11 make sure you knew that we had a copy of what we 12 previously produced and a -- and a new binder -- 13 MR. HEGARTY: Okay. 14 MR. TISI: -- to make things easy. 15 MR. HEGARTY: Thank you. 16 MR. TISI: Mm-hmm. 17 BY MR. HEGARTY: 18 Q Doctor, if you would turn to page 7 of 19 your report. 20 Are you there? 21 A Yes. 22 Q If you would look under the section 23 "Background: Underlying Opinions," Part 4, do you 24 see that part? 25 A Yes.</p> | <p style="text-align: center;">Page 222</p> <p>1 A Yes. 2 Q You say on page 7 of your report that 3 the grounds for this request from that Citizen 4 Petition included then the paragraphs you have 5 under -- under that part of your report. 6 Do you see where I'm referring to, 7 beginning with "Twelve publications"? 8 A Yes, I do. 9 Q And you say in your report: "Twelve 10 publications since 1995 confirming the causal 11 relationship between genital application of talc 12 and ovarian cancer and the protective effect of 13 tubal ligation or hysterectomy preventing the 14 translocation of talc to the ovary." 15 First of all, did you review the 12 16 publications that are at the back of Exhibit 13? 17 A I'm not -- I don't believe so, but I was 18 just summarizing the petition -- basis for their 19 petition. 20 Q Well, in your report, are you -- when 21 you refer to 12 publications, are you referring to 22 the 12 references that are at the back of 23 Exhibit 13? 24 A I'm simply summarizing what the petition 25 said. So they cited 12 studies, and I was just</p> |

4 (Pages 219 to 222)

April Zambelli-Weiner, Ph.D.

| Page 223 | Page 225 |
|---|---|
| <p>1 paraphrasing their basis for their petition.</p> <p>2 Q Well, where in the -- can you tell me</p> <p>3 where in the petition they make reference to 12</p> <p>4 publications since 1995 confirming the causal</p> <p>5 relationship between genital application of talc</p> <p>6 and ovarian cancer?</p> <p>7 A Sure. I believe that's paraphrased</p> <p>8 from -- let's see -- the second full paragraph on</p> <p>9 page 3.</p> <p>10 Q The paragraph beginning "The scientific</p> <p>11 basis"? Oh, I'm sorry, page 3.</p> <p>12 A Page 3.</p> <p>13 Q The paragraph beginning --</p> <p>14 A "Evidence" --</p> <p>15 Q -- "Evidence for the May 2008 petition."</p> <p>16 A Yes.</p> <p>17 Q So from that paragraph you made</p> <p>18 reference -- you -- you said that those 12</p> <p>19 publications in your report confirm the causal</p> <p>20 relationship between genital application of talc</p> <p>21 and ovarian cancer; is that correct?</p> <p>22 MR. TISI: Objection.</p> <p>23 THE WITNESS: Again, that's -- that's</p> <p>24 not my opinion. I'm simply paraphrasing the</p> <p>25 petition's basis.</p> | <p>1 THE WITNESS: Again, I would say that</p> <p>2 wasn't my -- my task or my charge, so, no, I did</p> <p>3 not do that.</p> <p>4 BY MR. HEGARTY:</p> <p>5 Q The next paragraph says: "An analysis</p> <p>6 of 16 pooled studies confirming a statistical --</p> <p>7 statistically significant 33 percent increased</p> <p>8 risk of ovarian cancer associated with perineal</p> <p>9 talc use."</p> <p>10 Did you make ref- -- did you review the</p> <p>11 reference they cited for that proposition?</p> <p>12 A That's a different question. Let me see</p> <p>13 what they cite.</p> <p>14 Q And I -- I can tell you they cite the</p> <p>15 Huncharek 2003 study.</p> <p>16 A I -- yes. I wanted to be sure. Well,</p> <p>17 then, yes, I did review that.</p> <p>18 Q So the Citizen Petition is using the</p> <p>19 Huncharek paper to advocate that there should be a</p> <p>20 warning for ovarian cancer with talcum powder use,</p> <p>21 correct?</p> <p>22 A I would say that's correct, they include</p> <p>23 that in their -- in their -- in their petition.</p> <p>24 Q So do you agree that they are using this</p> <p>25 paper to influence FDA to agree with their</p> |
| Page 224 | Page 226 |
| <p>1 BY MR. HEGARTY:</p> <p>2 Q But going back again to what I asked a</p> <p>3 moment ago, you did not go and confirm whether the</p> <p>4 12 publications they referenced actually do</p> <p>5 confirm a causal relationship between talc use and</p> <p>6 ovarian cancer?</p> <p>7 A No, that --</p> <p>8 MR. TISI: Objection.</p> <p>9 THE WITNESS: That wasn't my charge.</p> <p>10 MR. TISI: Objection. Outside the</p> <p>11 scope.</p> <p>12 Give me a moment to object.</p> <p>13 THE WITNESS: Sure. Sorry.</p> <p>14 BY MR. HEGARTY:</p> <p>15 Q With regard to the next paragraph</p> <p>16 concerning the -- or that begins with the</p> <p>17 statement "Strength of epidemiological evidence,"</p> <p>18 do you see that?</p> <p>19 A Yes.</p> <p>20 Q Again, did you review the references</p> <p>21 that you make in that paragraph to see if they did</p> <p>22 confirm the association between perineal talc use</p> <p>23 and the risk of ovarian cancer?</p> <p>24 MR. TISI: Objection. Outside the</p> <p>25 scope.</p> | <p>1 position?</p> <p>2 MR. TISI: Objection.</p> <p>3 THE WITNESS: I would agree that it is</p> <p>4 part of their submission to FDA. So to the extent</p> <p>5 that they're advocating for that position, it</p> <p>6 is -- it's part of that package, yes.</p> <p>7 BY MR. HEGARTY:</p> <p>8 Q Was it improper in your opinion for them</p> <p>9 to use the Huncharek paper to advocate for a</p> <p>10 warning of ovarian cancer with talcum powder</p> <p>11 product use?</p> <p>12 MR. TISI: Objection.</p> <p>13 THE WITNESS: I don't think I can really</p> <p>14 answer. I wasn't tasked with doing what they did,</p> <p>15 so I don't think I can really answer that question</p> <p>16 as to whether it was proper for them to do it or</p> <p>17 not to do it.</p> <p>18 BY MR. HEGARTY:</p> <p>19 Q Do you know what influence, if any, the</p> <p>20 2003 Huncharek paper had as part -- in connection</p> <p>21 with FDA's analysis of the Citizen Petition as</p> <p>22 submitted by Samuel Epstein?</p> <p>23 A I'm sorry. Can you repeat the question?</p> <p>24 Q Sure.</p> <p>25 A Thank you.</p> |

5 (Pages 223 to 226)

April Zambelli-Weiner, Ph.D.

| Page 227 | Page 229 |
|---|---|
| <p>1 Q Do you know -- do you happen to know 2 what influence, if any, the 2003 Huncharek paper 3 had in connection with FDA's analysis of the 4 Citizen Petition as submitted by Mr. Epstein?</p> <p>5 A I couldn't say specifically how much 6 weight they might have given it -- given to it, 7 other than that I would presume they reviewed it.</p> <p>8 Q You next cite a report by 19 scientists 9 in eight nations worldwide under IARC confirming a 10 30 to 60 percent increased risk of ovarian cancer 11 following the perineal application of talc.</p> <p>12 Is that a reference to the 2010 IARC 13 monograph, to your knowledge?</p> <p>14 A Again, I was just trying to paraphrase 15 their basis. So I'm not sure what -- it looks 16 like it is IARC, but they also cite a Lancet 17 paper.</p> <p>18 Q You did as part of your review, as you 19 mentioned, go back and review the 2010 IARC 20 monograph; is that correct?</p> <p>21 A I reviewed parts of it. I didn't -- 22 didn't read the whole thing.</p> <p>23 Q Now, IARC did not conclude that talc is 24 a carcinogen, correct?</p> <p>25 MR. TISI: Objection.</p> | <p>1 answer that because I wasn't really tasked with 2 reviewing the IARC report in detail and sort of 3 the basis for their conclusion. So I wouldn't 4 feel comfortable really answering that.</p> <p>5 BY MR. HEGARTY:</p> <p>6 Q In fact, as to IARC, you're aware that 7 it concluded that there was limited evidence of 8 carcinogenicity, but chance bias or confounding 9 could not be ruled out with reasonable confidence.</p> <p>10 MR. TISI: Objection.</p> <p>11 BY MR. HEGARTY:</p> <p>12 Q Do you recall reading that?</p> <p>13 MR. TISI: Objection.</p> <p>14 THE WITNESS: I don't recall reading 15 that specifically.</p> <p>16 BY MR. HEGARTY:</p> <p>17 Q At the top of page 8 of your report, you 18 make reference to the testimony of Ms. Loretz in 19 the first paragraph.</p> <p>20 Do you see that?</p> <p>21 A I'm looking.</p> <p>22 Q The middle of the paragraph.</p> <p>23 A Thank you.</p> <p>24 Yes, I see that.</p> <p>25 Q You say that, according to Ms. Loretz</p> |
| <p style="text-align: center;">Page 228</p> <p>1 THE WITNESS: I believe -- I mean, I'm 2 relying on recall here, but I believe they 3 concluded it was a 2B, possible human carcinogen.</p> <p>4 BY MR. HEGARTY:</p> <p>5 Q You're aware that they have categories 6 above that of probably carcinogenic and 7 carcinogenic?</p> <p>8 A Yes, I do.</p> <p>9 Q They did not characterize talc as 10 carcinogenic, correct?</p> <p>11 MR. TISI: Objection. Outside the 12 scope.</p> <p>13 THE WITNESS: Well, again, I would just 14 reiterate the 2B, possibly carcinogenic, 15 categorization.</p> <p>16 BY MR. HEGARTY:</p> <p>17 Q Which again, as you mentioned, is 18 possibly carcinogenic, correct?</p> <p>19 A That's their rubric, correct.</p> <p>20 Q IARC did not confirm that there was an 21 increased risk of ovarian cancer with application 22 of talc, correct?</p> <p>23 MR. TISI: Objection. Outside the 24 scope.</p> <p>25 THE WITNESS: I don't think I can really</p> | <p style="text-align: center;">Page 230</p> <p>1 that --</p> <p>2 MR. TISI: I think it's Dr. Loretz.</p> <p>3 MR. HEGARTY: Dr. Loretz. Okay.</p> <p>4 BY MR. HEGARTY:</p> <p>5 Q You say, according to Dr. Loretz, she 6 said that the PCP response was edited in meetings 7 with J&J and Imerys, and then you cite her 8 deposition at page 425.</p> <p>9 Do you see that?</p> <p>10 A Yeah, I'm just reading that sentence 11 again, please. (Peruses document.)</p> <p>12 Yes, I see that.</p> <p>13 MR. HEGARTY: I'm going to mark as 14 Exhibit 14 that page of Ms. Loretz's deposition.</p> <p>15 MR. TISI: Do you have the whole 16 deposition?</p> <p>17 MR. HEGARTY: I do, if you want to look 18 at it.</p> <p>19 MR. TISI: Would you mind, yeah. 20 (Exhibit No. 14 was marked for 21 identification.)</p> <p>22 BY MR. HEGARTY:</p> <p>23 Q You cited pages 4 -- 425/21, to 426/1. 24 Do you see where you made that reference, Doctor?</p> <p>25 A 425/21. Yes, I'm looking.</p> |

April Zambelli-Weiner, Ph.D.

| Page 231 | Page 233 |
|--|--|
| <p>1 Q Where does -- and my question is, where 2 does Ms. Loretz say in that portion of her -- her 3 deposition that you cited that the PCP response 4 was edited by J&J and Imerys?</p> <p>5 A So it doesn't say that, and I'm not sure 6 that's what I was conveying in that -- in that 7 sentence.</p> <p>8 It says, question: "This report was 9 written with Johnson & Johnson and Imerys's input, 10 correct?"</p> <p>11 And she says: "We probably had all of 12 our members who were interested, you know, review 13 it. That doesn't mean we changed the conclusions 14 at all."</p> <p>15 Q Right.</p> <p>16 A So I think I was simply referencing 17 that -- that it -- it was reviewed in consultation 18 with them.</p> <p>19 Q What is your support for saying that the 20 PCP response was prepared after edits and meetings 21 with J&J and Imerys?</p> <p>22 The only reference you make to support 23 that is this page from her deposition, and you 24 agree that there's no -- that this portion of the 25 deposition does not say that J&J and Imerys were</p> | <p>1 sentence, you say: "According to Dr. Linda 2 Loretz, director of Safety and Regulatory 3 Toxicology at PCPC, this document would have been 4 sent to the PCPC members for approval before 5 submission."</p> <p>6 Again, citing this same part of 7 Ms. Loretz's -- Ms. Loretz's testimony -- or 8 Dr. Loretz's testimony, where in the portion of 9 testimony that you cite does she say that it's 10 going to be sent to PCPC members for approval 11 before submission?</p> <p>12 A Again, I would say the same answer. 13 It's possible that it's a mistake in how the -- 14 how the deposition transcript is -- is cited, but 15 without seeing the rest of it, it's hard for me to 16 know.</p> <p>17 Q You say next on page 8 that: "The 2011 18 paper disclosed that the authors were consultants 19 for Johnson & Johnson and Imerys."</p> <p>20 Do you see in the second paragraph of 21 page 8 where you say that the 2011 article right 22 in the middle, that you -- you refer to the title, 23 and then you say, "... and discloses that the 24 authors were consultants to Johnson & Johnson and 25 Imerys at the time the initial drafts of this</p> |
| Page 232 | Page 234 |
| <p>1 involved in editing the PCP response, does it?</p> <p>2 MR. TISI: Objection. You -- it 3 misstates her testimony. You know that -- you 4 know what her testimony was.</p> <p>5 BY MR. HEGARTY:</p> <p>6 Q You can go ahead and respond.</p> <p>7 A Again, I -- this is just one section, 8 and I know I cite other sections, so I'm a little 9 uncomfortable responding fully in the absence of 10 the full document. But I can simply say that I 11 think my intention was to cite that -- that there 12 was collaboration with J&J or Imerys or at least 13 the opportunity to review.</p> <p>14 Q Well, then, where did you get the 15 information from on which you base the statement 16 "after edits and meetings with J&J and Imerys"?</p> <p>17 A Do you have the rest of the -- the other 18 cites for the Loretz dep?</p> <p>19 Q Well, you think that it might be in 20 those other cites?</p> <p>21 A It just would give me a fuller picture 22 of -- of what I was trying to convey in this 23 paragraph.</p> <p>24 Q Well, we'll come back to that.</p> <p>25 If you look at the next section -- next</p> | <p>1 manuscript was produced."</p> <p>2 Do you see where I'm reading?</p> <p>3 A I do.</p> <p>4 Q I'm going to mark as Exhibit 15 the 2011 5 paper. 6 (Exhibit No. 15 was marked for 7 identification.)</p> <p>8 MR. TISI: Thank you.</p> <p>9 BY MR. HEGARTY:</p> <p>10 Q If you turn to the very last page -- I'm 11 sorry, if you turn to page 506, do you see the 12 "Acknowledgments," "Conflicts of Interest" 13 section?</p> <p>14 A I do, yes.</p> <p>15 Q The authors don't cite that they were 16 consultants of Johnson & Johnson and Imerys at the 17 time the initial drafts of the manuscript were 18 produced, do they?</p> <p>19 A That's correct. It just says "Johnson & 20 Johnson Consumer Product Worldwide."</p> <p>21 Q So your reference to Imerys is a 22 mistake, correct?</p> <p>23 A It may be. With regard to this specific 24 COI and the exact wording, yes, I would say that's 25 correct.</p> |

April Zambelli-Weiner, Ph.D.

| Page 235 | Page 237 |
|--|--|
| <p>1 Q Thank you. 2 Now, throughout your paper -- I'm sorry, 3 throughout your report, you do not distinguish 4 between citations to footnotes and citations to 5 the references to the work cited. For example, if 6 you go to page 11 of your report, at the very top 7 you make reference to a footnote 5 that refers to 8 the PRISMA statement, but then in the following 9 paragraph, in the same format as a footnote, you 10 make reference to 16. 11 Do you see that? 12 MR. TISI: I'm sorry, where are you, 13 Counsel? I -- 14 BY MR. HEGARTY: 15 Q The top of page 11, there's a footnote 5 16 that appears to refer to a PRISMA statement. Then 17 the -- the next line after that footnote beginning 18 "The 2009 paper" ends with a reference to 16. 19 Is 16 a footnote as well? 20 A No. If it was a footnote, it would be 21 on that page. 22 Q So what is the reference to -- to 16? 23 A It should be in the back. Let's take a 24 look. (Peruses document.) 25 So it is a reference 16 in the work</p> | <p>1 (Exhibit No. 16 was marked for 2 identification.) 3 BY MR. HEGARTY: 4 Q This is obviously one of the papers that 5 was a focus of your report, correct? 6 A Correct. 7 Q If you look on page 14, of your report 8 under the section "Analysis" beginning at "6.1 9 Huncharek, et al., 2003." Do you see where I'm 10 referring you to? 11 A Yes. 12 Q In the first line you say: "In 2003, a 13 meta-analysis study by Huncharek, Geschwind and 14 Kupelnick -- Kupelnick." Do you see where I'm 15 reading? 16 A Yes, I do. 17 Q If you look at the first page of the -- 18 of the Exhibit 16, you misspelled Geschwind, did 19 you not? 20 A Yes, it appears I did. 21 Q If you look over on page 18 of your 22 report under the section "Lack of replication, 23 2003 Huncharek Meta-analysis," do you see where 24 I'm referring you to? 25 A Yes, I do.</p> |
| <p style="text-align: center;">Page 236</p> <p>1 cited. 2 Q So is it proper format to make reference 3 to footnotes and make references to the work cited 4 using the same format? 5 MS. PARFITT: Objection to form. 6 MR. TISI: Objection. 7 THE WITNESS: I think it is. I mean, I 8 think, could it have been clearer, sure, but I 9 don't think there's -- there's anything wrong with 10 doing that. 11 BY MR. HEGARTY: 12 Q Have you ever done -- used that kind of 13 format in any published work of yours? 14 MR. TISI: Objection. 15 THE WITNESS: I don't recall. 16 BY MR. HEGARTY: 17 Q You do agree that it can be confusing. 18 A Sure. I mean, generally footnotes are 19 on the same page, and, you know, I think you can 20 follow the pattern there, but you certainly could 21 use another format to make it a little bit 22 clearer. 23 Q I'm going to mark as Exhibit 16 the 2003 24 Huncharek paper, which I'm sure you have a copy of 25 as well.</p> | <p>1 Q You begin that section by saying: "In 2 their 2003 paper, Drs. Huncharek and Muscat 3 claim." Do you see where I'm reading? 4 A Yes. 5 Q Dr. Muscat was not an author on the 2003 6 paper, was he? 7 MR. TISI: Objection. 8 THE WITNESS: He was not an author, but 9 I believe I'm referencing my understanding that he 10 worked on the paper in some capacity. 11 BY MR. HEGARTY: 12 Q Well, from -- what is your basis for 13 saying that he in some way worked on this paper? 14 A If I'm recalling correctly, I'm thinking 15 about his deposition. 16 Q But if you read his deposition, you know 17 that he said that he had no involvement in this 18 paper, correct? 19 MR. TISI: Objection. 20 THE WITNESS: I don't -- I don't recall 21 his deposition word for word. 22 BY MR. HEGARTY: 23 Q Well, throughout your report when you 24 refer to the 2003 study, you continually refer to 25 this study as by Huncharek and Muscat, don't you?</p> |

April Zambelli-Weiner, Ph.D.

| Page 239 | Page 241 |
|--|---|
| <p>1 A I do. And, you know, I'm also 2 recalling, hopefully correctly, that they were 3 both named on the proposal. Again, I don't have 4 the documents in front of me, but my recollection 5 is that they may have both been named on the 6 proposal and the preliminary report from which 7 some of the data in the 2003 paper derived from. 8 Q But, Doctor, in the section I'm pointing 9 to and throughout your report, you are referring 10 to and critiquing the 2003 article we marked as 11 Exhibit No. 16, correct? 12 A That's correct. 13 Q So it would be a mistake to -- when 14 you're talking about this article, to say that 15 Dr. Muscat was an author of this article, correct? 16 MR. TISI: Objection. She already 17 answered that question. Asked and answered. 18 You can go ahead and answer. 19 BY MR. HEGARTY: 20 Q You can answer. 21 A Again -- 22 MR. TISI: You can answer again. 23 THE WITNESS: Okay. Yeah, I believe I'm 24 referencing his involvement in -- in the data in 25 the paper.</p> | <p>1 before. 2 BY MR. HEGARTY: 3 Q So you don't consider that to be a 4 mistake in your report? 5 A I don't, no. 6 Q If you would turn over to Table 1 on 7 page 15 of your report. Tell me when you're 8 there. 9 A Okay. 10 Q First, in footnote 8, you note that 11 typographical and grammatical errors can and do 12 occur in research, correct? 13 A Correct. 14 Q These can include transcription errors 15 where data is inadvertently transferred 16 incorrectly, correct? 17 A I don't believe that's what I said. 18 Q But do you agree that typographical and 19 grammatical errors in a publication can include 20 transcription errors where data is inadvertently 21 transferred incorrectly? 22 MR. TISI: Objection to the term 23 "transcription errors." 24 THE WITNESS: Well, again, I don't know 25 how -- I don't know exactly how you're using</p> |
| <p style="text-align: center;">Page 240</p> <p>1 BY MR. HEGARTY: 2 Q So you don't think it's a mistake when 3 you're talking about the 2003 paper with lead 4 author Huncharek to continually talk about 5 Dr. Muscat as an author of that paper. 6 MR. TISI: Objection. 7 THE WITNESS: Again, I think my 8 characterization of it is -- you know, as you can 9 see in the title above it, "2003 Huncharek 10 Meta-analysis," and then below citing his 11 involvement in the paper -- 12 BY MR. HEGARTY: 13 Q But you -- 14 A -- and the data. 15 Q But you are saying that in the first 16 sentence: Drs. Huncharek and Muscat claim that 17 their calculations suggest an inverse 18 dose-response relationship." 19 There you're referring to what they're 20 claiming in the 2003 paper, correct? 21 MR. TISI: Objection. Asked and 22 answered. 23 THE WITNESS: Again, the dose-response 24 data actually appears prior in a 2000 report. So, 25 again, I would stay by my statement, sir, from</p> | <p style="text-align: center;">Page 242</p> <p>1 "transcription." Perhaps you can clarify. 2 BY MR. HEGARTY: 3 Q Well, can errors in -- do errors in the 4 transfer of data sometimes occur in publications? 5 A Sure. Yes. 6 Q Do citation errors sometimes occur in 7 publications? 8 A Yes. 9 Q Is it your methodology for purposes of 10 your report that any article or study with 11 typographical, grammatical or citation errors 12 renders that study invalid? 13 A No, I don't think -- 14 MR. TISI: Let me just place an 15 objection. 16 THE WITNESS: Sorry. 17 MR. TISI: Thank you. 18 THE WITNESS: I'm sorry. 19 BY MR. HEGARTY: 20 Q You can answer. 21 A Could you repeat the question. Thank 22 you. 23 Q Is it your methodology for purposes of 24 your report that any article or study with 25 typographical and grammatical or citation errors</p> |

April Zambelli-Weiner, Ph.D.

| Page 243 | Page 245 |
|---|--|
| <p>1 renders that study invalid?</p> <p>2 A No, I don't think that's what I'm saying</p> <p>3 at all. I think that I'm talking about an</p> <p>4 analysis of internal validity of a study for which</p> <p>5 there are, you know, numerous components to that.</p> <p>6 Q But you state in that footnote that:</p> <p>7 "The number of errors identified in this paper</p> <p>8 raise concerns about the rigor of the authors'</p> <p>9 quality control procedures and the editorial</p> <p>10 review process for this journal."</p> <p>11 Do you see where I'm reading?</p> <p>12 A I do.</p> <p>13 Q Can you identify for me any written</p> <p>14 standard for the number and type of errors that</p> <p>15 are recognized to raise concern about the rigor of</p> <p>16 the authors' quality control procedures? Is there</p> <p>17 any objective standard published?</p> <p>18 MR. TISI: Objection.</p> <p>19 THE WITNESS: That was a long question.</p> <p>20 I'm going to do my best to answer it. It was</p> <p>21 compound.</p> <p>22 So there are certainly standards about</p> <p>23 the types of errors, and I believe that was one of</p> <p>24 the components of what you said. And I would</p> <p>25 refer you to IARC actually for a good example of</p> | <p>1 textbook. And I -- I'm sure there are many others</p> <p>2 related to specifically substantive errors which</p> <p>3 are really critical in a meta-analysis. Because a</p> <p>4 meta-analysis, by definition, is an analysis of</p> <p>5 other people's studies and other people's data.</p> <p>6 And so when you're assessing a question of</p> <p>7 validity, the question is, are you measuring what</p> <p>8 you say you're measuring, and you're either</p> <p>9 measuring the data from the prior studies</p> <p>10 accurately or you're not. So that drives directly</p> <p>11 at validity.</p> <p>12 Q Have you ever published in any article</p> <p>13 or journal the number of errors in a paper that</p> <p>14 raise concerns that -- the number of errors that</p> <p>15 are necessary to raise concerns about the rigor of</p> <p>16 the authors' quality control procedures and</p> <p>17 editorial review process?</p> <p>18 A Can you repeat that question, please?</p> <p>19 Q Sure.</p> <p>20 Have you ever published in a journal or</p> <p>21 any -- or in any format the number of errors it</p> <p>22 takes before you have concerns about the rigors of</p> <p>23 the authors' quality control or the editorial</p> <p>24 review process? Is there an objective number?</p> <p>25 Five errors? Ten errors?</p> |
| Page 244 | Page 246 |
| <p>1 that in terms of when there is lack of clarity or</p> <p>2 lack of transparency or these types of issues,</p> <p>3 that it does call into question the quality of the</p> <p>4 paper, and therefore could impact the weight that</p> <p>5 such a paper is given in a weight-of-evidence</p> <p>6 analysis or a causation analysis.</p> <p>7 So I think that, you know, when we're</p> <p>8 talking about something like this that is a</p> <p>9 meta-analysis, you know, there absolutely are --</p> <p>10 are guidances and standards around the kinds of</p> <p>11 errors and the importance of precise abstraction</p> <p>12 of data from the original studies.</p> <p>13 BY MR. HEGARTY:</p> <p>14 Q Can you point to me to any such</p> <p>15 published guidance and standards?</p> <p>16 A I think I just mentioned one. I think</p> <p>17 when we met last time --</p> <p>18 Q I'm sorry, when you say IARC, are you</p> <p>19 talking about the monograph?</p> <p>20 A Sure. Because they -- they discuss</p> <p>21 methodology --</p> <p>22 Q Okay.</p> <p>23 A -- in part of the IARC monograph.</p> <p>24 I think I mentioned before the Cochran</p> <p>25 collaboration. I think I mentioned the Bornstein</p> | <p>1 A I have not published on that. I don't</p> <p>2 know that anyone has. And I'm not even sure that</p> <p>3 would be appropriate because it's really, again,</p> <p>4 about a wholistic analysis of the internal</p> <p>5 validity of a study, and -- and that you can't</p> <p>6 take really individual errors out of that -- out</p> <p>7 of that larger context, or just not all errors are</p> <p>8 also created equally.</p> <p>9 Q What does it take for an error in a</p> <p>10 publication to be a substantive error in your</p> <p>11 opinion?</p> <p>12 A Well, in my opinion, it would depend</p> <p>13 on --</p> <p>14 MR. TISI: Let me just object to the</p> <p>15 vagueness of the question.</p> <p>16 Go ahead.</p> <p>17 THE WITNESS: Sure.</p> <p>18 In my opinion, it would depend on the</p> <p>19 nature of the study or the nature of the</p> <p>20 publication. I think in meta-analysis, I would</p> <p>21 definitely consider misabstraction or</p> <p>22 misrepresentation of the data from the original</p> <p>23 studies, particularly under the premise of a -- of</p> <p>24 a protocol that involves double abstraction, a --</p> <p>25 a concerning and substantive error.</p> |

April Zambelli-Weiner, Ph.D.

| Page 247 | Page 249 |
|---|--|
| <p>1 BY MR. HEGARTY:</p> <p>2 Q Can you identify for me any other types 3 of errors in a publication that you consider 4 substantive errors besides what you just provided?</p> <p>5 A Well, I -- I think I detail a lot of 6 them, you know, in -- in my report.</p> <p>7 Q Well, let us talk about those then.</p> <p>8 MR. TISI: I'm sorry, she wasn't 9 finished with her answer, Counsel. You asked her 10 a question, unless you are withdrawing the 11 question.</p> <p>12 MR. HEGARTY: No, I'm not withdrawing.</p> <p>13 BY MR. HEGARTY:</p> <p>14 Q Did you finish?</p> <p>15 A Can you repeat the question, please?</p> <p>16 Q Well, yeah, I had asked you about, 17 can you identify for me any other types of errors in 18 a publication that you consider substantive errors 19 besides what you provided, and I was going to then 20 allow you to make reference to what you include in 21 your report, but if you want to go ahead and give a 22 separate response, that's fine.</p> <p>23 A I lost my train of thought. I -- I 24 think I was -- I was going to say that obviously I 25 detailed, you know, some of these in my report,</p> | <p>1 substantiate it. It can't be replicated. That's 2 what you say, correct?</p> <p>3 A Correct.</p> <p>4 Q That's not true, is it?</p> <p>5 A Well, that is my analysis of -- of that 6 particular statement.</p> <p>7 Q Well, do you have the paper in front of 8 you, Exhibit 16?</p> <p>9 A Yes, I do.</p> <p>10 Q If you turn to the references, do you 11 see there's a reference there to 3, Cooper & 12 Hedges, L.V., The Handbook of Research Synthesis, 13 New York, Russell Sage Foundation, 1994?</p> <p>14 Do you see that reference?</p> <p>15 A I see that reference, but I just --</p> <p>16 Q Do you --</p> <p>17 A Excuse me, I want to --</p> <p>18 MR. TISI: Give her a moment.</p> <p>19 THE WITNESS: I want to find the section 20 of the paper where that particular statement comes 21 from. (Peruses document.)</p> <p>22 BY MR. HEGARTY:</p> <p>23 Q You list it as page 1956, paragraph 2.</p> <p>24 A Thank you.</p> <p>25 MR. TISI: And if you have -- on your</p> |
| <p>1 and I think that -- again, I would just reiterate, 2 it really depends upon the nature of the error and 3 the paper and the study.</p> <p>4 Q So if we look at the sentence just 5 before Table 1, you say: "A list of substantive 6 errors is provided in Table 1 of this report 7 (below)."</p> <p>8 Do you see where I'm reading?</p> <p>9 A I do.</p> <p>10 Q So in your opinion, the errors -- the 11 references that you cite in Table 1 are those you 12 consider to be substantive errors, correct?</p> <p>13 A I would say, correct, within the context 14 of my footnote, which is, you know, trying to 15 distinguish between, you know, more typographical 16 and grammatical errors versus errors that drive at 17 the -- the methods or the results of the study.</p> <p>18 Q Well, let's go through them one by one. 19 Let's look at the first one. You quote the 2003 20 article as saying, "Literature retrieval was 21 performed by previously described methods," 22 quoting 8. Correct?</p> <p>23 A Correct.</p> <p>24 Q You say, though, that Citation 8 is not 25 correct, so there was no method provided to</p> | <p>1 note, if you have your report with --</p> <p>2 THE WITNESS: Yes. Thank you for that 3 reminder, yeah.</p> <p>4 MR. TISI: Sure.</p> <p>5 THE WITNESS: I'll have to keep -- maybe 6 I'll -- maybe I'll switch to that report, that 7 version of the report.</p> <p>8 BY MR. HEGARTY:</p> <p>9 Q We're on page 15.</p> <p>10 MR. TISI: I think you said you had the 11 references pulled out of the report with the --</p> <p>12 THE WITNESS: Right. Yeah.</p> <p>13 MR. TISI: Okay.</p> <p>14 THE WITNESS: Right. So in the paper 15 they cite to that statement with -- with -- let me 16 see, I'm trying to find it -- with -- with 17 reference 8. So you're referring to reference 3?</p> <p>18 BY MR. HEGARTY:</p> <p>19 Q Correct. Did you read reference 3?</p> <p>20 A Which -- which, by the way, my 21 understanding is an entire textbook. Just let me 22 confirm.</p> <p>23 Right. So in my opinion, it -- it's 24 really not appropriate to cite an entire 25 textbook -- or let's just say it's -- it's not</p> |

April Zambelli-Weiner, Ph.D.

| Page 251 | Page 253 |
|---|---|
| <p>1 informative to cite an entire textbook for 2 literature retrieval methods. 3 Typically the way that's handled in 4 research is, if you've published a prior study 5 where you've provided a lot of detail on your 6 protocol, because papers are like -- word count is 7 prime real estate in a -- in a peer-reviewed 8 paper, you take advantage of that and you go ahead 9 and reference the prior paper so you don't have to 10 go through that again. So that's really standard. 11 I find this to be not informative about 12 the literature retrieval method to cite an entire 13 textbook. 14 Q So do -- would you find it to be a 15 substantive error if they meant to make reference 16 to -- to number 3 instead of number 8, if that -- 17 THE REPORTER: I couldn't hear you. You 18 have got -- I need you to finish your question. I 19 didn't hear it with the cough. Sorry. 20 MR. HEGARTY: Okay. 21 BY MR. HEGARTY: 22 Q All right. Would you consider a -- a 23 typographical error where they meant to refer to 3 24 but they said 8 as a substantive error? 25 MR. TISI: Objection.</p> | <p>1 be -- the way they described the databases that 2 they've searched definitely left me with questions 3 as -- excuse me -- as well as the search terms. 4 That's not really a very detailed way of -- of 5 laying out your search terms. So I disagree with 6 your assessment. 7 Q Well, it would be -- it would be 8 incorrect to say that they made no description at 9 all of how they did their literature retrieval, 10 correct? 11 A I'm sorry. Repeat, please. 12 Q Sure. It would be incorrect to say that 13 the authors made -- provided no description of how 14 they went about doing their literature retrieval, 15 correct? 16 A I think I would agree. Obviously, they 17 provide some description, but whether that's 18 adequate and informative, I think that's a 19 different question. 20 Q Was it your contention that their -- the 21 way they provided the information as to the 22 literature retrieval method was a substantive 23 error in their report? 24 A Well, again, I think -- yes, I think 25 I -- I think I've said that in Table 1, just that</p> |
| Page 252 | Page 254 |
| <p>1 THE WITNESS: Well, I think I'm going to 2 stand by what I put in my table, which is 3 methods -- references are important, and if 4 they're relying on another reference for their 5 method, then it should be informative as to the 6 method in a way that someone could replicate their 7 meta-analysis if they -- if they so desired. 8 BY MR. HEGARTY: 9 Q But -- in that very same section that 10 you reference, in 1956, the authors go on and 11 describe in quite -- in a quite detailed way the 12 way they did their literature search, didn't they? 13 A Well, I'm going to take a quick look 14 just to refresh my memory. (Peruses document.) 15 I -- I don't think I would agree with 16 your characterization of that. 17 Q Well, they -- they reference the 18 databases that they searched, correct? 19 A They do, but it's very -- it's a very 20 odd and very strange reference that leaves me with 21 a lot of questions. Because the MEDLARS 22 reference -- MEDLARS is a several iterations ago 23 version of PubMed. So MEDLARS hasn't been MEDLARS 24 since, I don't know, a long time ago. 25 So I found it very strange for them to</p> | <p>1 it's -- it drives directly at the methods of the 2 meta-analysis. So in that way, I consider it a 3 substantive error. 4 Q Well, what would have changed in the 5 report if they had provided a different 6 description of the -- their literature retrieval 7 methods? 8 A I -- I can't answer that. I would've 9 had to see what they changed. 10 Q Is there a written authority that -- 11 that tells authors on how they're to describe 12 in -- in their articles how they do their 13 literature search and how to cite it? 14 A I -- there very well may be. I think 15 there's certainly convention for anyone who is 16 well versed in -- in the field. 17 Q Can you cite for me any published 18 authority that tells authors how they're to 19 describe their literature searches? 20 MR. TISI: Objection. 21 THE WITNESS: Not off the top of my head 22 as I sit here, but that doesn't mean it doesn't 23 exist. 24 BY MR. HEGARTY: 25 Q Your second point in that table --</p> |

April Zambelli-Weiner, Ph.D.

| Page 255 | Page 257 |
|--|--|
| <p>1 MR. TISI: Table 1 from --</p> <p>2 MR. HEGARTY: Table 1. We're going to</p> <p>3 stick with Table 1 for the next 30 or 40 minutes</p> <p>4 at least.</p> <p>5 MR. TISI: Okay.</p> <p>6 BY MR. HEGARTY:</p> <p>7 Q -- refers to text, noting that the</p> <p>8 Hankinson data was subsequently used in Gertig so</p> <p>9 that Gertig would only be included, but then you</p> <p>10 note that they went on to cite 12, or Hankinson,</p> <p>11 instead, correct?</p> <p>12 A Right. So I believe -- just to make</p> <p>13 sure I'm understanding your characterization</p> <p>14 correctly, in the text they say Hankinson was</p> <p>15 included and Gertig was removed, but in Table 1</p> <p>16 where they list the studies that were included,</p> <p>17 Hankinson is not there and Gertig is there.</p> <p>18 Q Correct. So the table is correct,</p> <p>19 right?</p> <p>20 A Well, I think it -- it leaves -- it</p> <p>21 leaves an open question. I mean we -- we can take</p> <p>22 that at face value and assume that that's --</p> <p>23 that's what happened, but, you know, certainly</p> <p>24 that's a question.</p> <p>25 Q Well, they say that the Hankinson data</p> | <p>1 THE WITNESS: Not necessarily, and I'll</p> <p>2 tell you why. Because usually there is a graph --</p> <p>3 a graphical depiction of, you know, a forest plot</p> <p>4 of the results of the meta-analysis. That's a</p> <p>5 very standard reporting out of your results.</p> <p>6 And in that graph, you get really</p> <p>7 important information about the meta-analysis.</p> <p>8 You know which studies were actually used, you get</p> <p>9 the point estimates, the confidence intervals, you</p> <p>10 often gets the weights that were applied to those</p> <p>11 studies. And so that would have been confirmatory</p> <p>12 of which study was in fact actually used. So</p> <p>13 since that doesn't appear here, it's an open</p> <p>14 question.</p> <p>15 BY MR. HEGARTY:</p> <p>16 Q Well, if they had said only reference 10</p> <p>17 was included in the meta-analysis, would you have</p> <p>18 said that that's a -- a problem or an issue?</p> <p>19 MR. TISI: Objection.</p> <p>20 THE WITNESS: I'm sorry. Can you repeat</p> <p>21 that, please?</p> <p>22 BY MR. HEGARTY:</p> <p>23 Q Sure. If they had said therefore only</p> <p>24 reference 10 was included in the meta-analysis,</p> <p>25 instead of saying reference 12, would you have</p> |
| Page 256 | Page 258 |
| <p>1 was included in Gertig, so they would use Gertig.</p> <p>2 And the mistake you're pointing out is that in the</p> <p>3 text they actually say we're taking -- we're going</p> <p>4 to refer to Hankinson, correct?</p> <p>5 A I'm having a hard time reading it. Let</p> <p>6 me look here. One second. (Peruses document.)</p> <p>7 Q In other words, they say that --</p> <p>8 A Right.</p> <p>9 Q -- they're going to go with Gertig, but</p> <p>10 then they say they're go -- then they make</p> <p>11 reference to 12, which is Hankinson, instead of</p> <p>12 10, correct?</p> <p>13 A Correct. So they say 12 was included,</p> <p>14 and therefore only 12, which is Hankinson was</p> <p>15 included in the meta-analysis. But in Table 2, it</p> <p>16 looks like it was Gertig and -- and not Hankinson,</p> <p>17 although --</p> <p>18 Q So any -- I'm sorry.</p> <p>19 A -- we can't be sure what actually</p> <p>20 happened.</p> <p>21 Q But anyone reading this paper when they</p> <p>22 looked at Table 1 would know that that's a</p> <p>23 typographical error, that they meant to say</p> <p>24 citation 10, Gertig, correct?</p> <p>25 MR. TISI: Objection.</p> | <p>1 also called that a substantive error?</p> <p>2 MR. TISI: Objection.</p> <p>3 THE WITNESS: Well, I think -- I think</p> <p>4 certainly that would have improved the situation.</p> <p>5 I mean it doesn't -- you know, it wouldn't have</p> <p>6 drawn this direct contradiction that leaves an</p> <p>7 open question that's not answered by the lack</p> <p>8 of -- of reporting out on the meta-analysis</p> <p>9 results. So -- but obviously having the graphical</p> <p>10 report out of the meta-analysis results would have</p> <p>11 resolved that question.</p> <p>12 BY MR. HEGARTY:</p> <p>13 Q Anyone looking at Table 2 would see that</p> <p>14 Gertig was included and not Hankinson, correct?</p> <p>15 A Again, you know, there are other errors</p> <p>16 in Table 1. So, you know, again, it's an open</p> <p>17 question. I'm not going to agree that you can</p> <p>18 assume that that's what happened because, you</p> <p>19 know, there's other errors.</p> <p>20 Q And I said Table 1, I meant -- Table 2,</p> <p>21 I said. I meant to say Table 1. Well --</p> <p>22 MR. TISI: Table 1 -- I guess where I'm</p> <p>23 confused here, are you talking about Table 1 from</p> <p>24 the report or the table from the -- from the</p> <p>25 article?</p> |

April Zambelli-Weiner, Ph.D.

| Page 259 | Page 261 |
|---|--|
| <p>1 MR. HEGARTY: Well, please, Chris, I 2 understand -- 3 MR. TISI: Well -- 4 MR. HEGARTY: If I make an error -- an 5 issue with the clarity of the -- of the 6 transcript, I'd just rather you not take my time 7 with asking questions. 8 MR. TISI: I -- I'll give you an extra 9 20 seconds. 10 Can you tell me which chart -- which 11 chart you're referring to? 12 MR. HEGARTY: My question was, as it 13 relates to Table 1, anyone in the article, the 14 2003 article would know that they included Gertig 15 and not Hankinson. 16 BY MR. HEGARTY: 17 Q Correct, Doctor? 18 A Oh, I'm sorry. I didn't realize you 19 were asking me -- 20 Q Sure. 21 A -- a question again. Go ahead. 22 Q In Table 1 of the -- of the 2003 23 article, they don't reference Hankinson, correct? 24 A That is correct. 25 Q And in fact, it was proper to include --</p> | <p>1 contradictions in the context of other errors 2 within this paper, including in Table 1, coupled 3 with the lack of reporting out on the results of 4 the meta-analysis, which would resolve the 5 contradiction, leave it as an open question. 6 Q Your third point in Table 1 of your 7 report on page 15 refers to the authors reporting 8 on the lowest dose and how Booth had a lowest dose 9 of rarely or less-than-one-time dose that's not 10 reported, correct? 11 A Correct. That's correct. 12 Q And you know that this was not included 13 because a rarely or less-than-one-month -- 14 one-per-month-dose could not be combined with the 15 other study data. You know that's why the authors 16 didn't list that, correct? 17 MR. TISI: Objection. Calls for 18 speculation. 19 THE WITNESS: I -- I don't know that, 20 and I think that that -- that's exactly the point. 21 If you look at the study, and I'm just 22 trying to flip to the section in the study, I 23 believe there was like a one-line description of 24 the dose-response analysis. 25 But I think it's important to find it.</p> |
| <p style="text-align: center;">Page 260</p> <p>1 include Gertig and not Hankinson because Gertig 2 had used the same data, correct? 3 A Well, I -- I didn't do that analysis. I 4 mean, I assume that's -- that's their judgment or 5 what they're trying to convey, but, you know, I 6 sort of stand by the position that that's an open 7 question as to what was actually done. 8 Q Well, how did this excerpt with errors, 9 as you say it, in Table 1 of your report have any 10 substantive impact on the article? 11 A Oh, I mean I think what studies were 12 included in the meta-analysis absolutely is -- you 13 know, drives at the core of this -- of the paper 14 and the -- the substance of this paper. 15 Q Well, Doctor, at the top of Table 1 in 16 the 2003 paper, they say "Overview of included 17 studies." That means these are the studies they 18 included in the meta-analysis, correct? 19 A That is what it says, correct. 20 Q So how did a misreference to Hankinson 21 in that paragraph when Hankinson is not included 22 here have any substantive effect on the paper? 23 A I think I answered your question, but 24 I'll go ahead -- I'll go ahead and say it again. 25 Those types of contradictory errors or</p> | <p style="text-align: center;">Page 262</p> <p>1 Because the authors basically state that the 2 lowest recorded exposure category -- a comparison 3 was made across these studies comparing the lowest 4 recorded exposure category with the highest 5 exposure level. That is the extent of their 6 methods description related to their dose-response 7 analysis. 8 So, if you take them at face value that 9 what they're saying is true, you go back to the 10 original studies and you look for the lowest 11 recorded exposure category, and that is not what 12 they did. 13 BY MR. HEGARTY: 14 Q Would you have any problem if this 15 article -- the 2003 article had recorded that 16 we're not including the rarely or 17 less-than-one-month from Booth because we couldn't 18 combine it with the other studies data? 19 A Well, I think certainly what I can agree 20 to is that a more -- a more detailed transparent 21 methods description of what actually was done 22 would have been very appreciated and welcomed, and 23 I think at that point, you know, I would evaluate 24 that on -- on its merits. But that's not what 25 happened, so it leaves us with a lot of questions.</p> |

April Zambelli-Weiner, Ph.D.

| Page 263 | Page 265 |
|--|--|
| <p>1 And I also -- I also think, excuse me, 2 just to add, that it's misleading. Because if 3 someone comes in -- comes in to this paper and is 4 not familiar with this body of literature and with 5 these studies, then it looks like these are the -- 6 the exposure categories that are reported out for 7 each of these studies, when in fact that's not 8 accurate. That's not a full and accurate 9 characterization of the data in these underlying 10 studies.</p> <p>11 Q You figured it out. You -- you aren't 12 contending that others couldn't pull the Booth 13 paper and figure it out, are you?</p> <p>14 A Again, it's about standards of 15 methods -- no one should have to, right? It 16 should be very clearly spelled out exactly what 17 they are doing. Methods have to be spelled out; 18 decisions have to be justified.</p> <p>19 That's -- you know, what you're alleging 20 is -- presuming that is what happened, is -- is a 21 methodologic choice that the authors are making 22 that they're obligated to describe and justify to 23 a certain extent, and that did not happen.</p> <p>24 Q As a general proposition, though, it's 25 not improper in a meta-analysis if you have some</p> | <p>1 we shouldn't be in that position of having to 2 guess and wonder what they did or make 3 assumptions, and I think that that's the point, 4 and that's really the -- the most I can say about 5 that.</p> <p>6 Q So did you actually go back and read the 7 Booth paper?</p> <p>8 A I did, yes.</p> <p>9 Q And from reading the Booth paper, you 10 did not conclude that they excluded that rarely or 11 less-than-one-time per dose because it -- no -- no 12 such similar data was collected across the other 13 studies? Did you not make note of that?</p> <p>14 MR. TISI: Objection.</p> <p>15 THE WITNESS: I simply made note of what 16 they did. What I can say is, first of all, I 17 don't prescribe to the premise that -- that this 18 dose-response analysis is valid at face value. 19 Just the methodologic choices made by the author. 20 So let's just establish that, put that aside.</p> <p>21 There are lots of different ways to do 22 this, to do -- to do a dose-response analysis, to 23 do a meta-analysis, and so I can't really 24 speculate on what they thought they were doing or 25 what they actually did. I think all I can say is</p> |
| <p>1 parts of data you can't combine with other -- with 2 data from other studies to just include the data 3 across the studies that you can combine, correct?</p> <p>4 A I'm sorry. Can you read that back or 5 rephrase?</p> <p>6 Q Sure. As a general proposition, it's 7 not improper in a meta-analysis if you have some 8 parts of data you can't combine with other studies 9 to then just include the data across the studies 10 that you can combine, correct?</p> <p>11 MR. TISI: Object.</p> <p>12 BY MR. HEGARTY:</p> <p>13 Q That you're matching like with like or 14 combining like with like.</p> <p>15 A Again, that's a very sort of amorphous, 16 abstract question, but I'll -- I'll do my best to 17 answer it.</p> <p>18 I mean, I think, you know, that when 19 you're doing a meta-analysis, you should set out 20 the research questions, set out the objective, set 21 out the inclusion/exclusion criteria, make that 22 very clear, and describe the methods, describe 23 your justification for your choices, and then 24 allow the reader to evaluate those.</p> <p>25 Again, I don't know what they did, and</p> | <p>1 they had an obligation to lay that out and allow 2 people to evaluate it and were -- were unable to 3 do that.</p> <p>4 BY MR. HEGARTY:</p> <p>5 Q How did this present or how did this -- 6 strike that.</p> <p>7 How was this a substantive error that 8 affected the results or conclusions of the 2003 9 paper?</p> <p>10 A Again, it drives directly to the methods 11 and the results of the study. If you say you are 12 taking the lowest recorded exposure category from 13 each study, then that should be an accurate 14 statement, and it's not an accurate statement. If 15 you did something else, then you should describe 16 that something else, and you should justify that 17 something else so that people can evaluate the 18 validity of that, the risk of bias of that and so 19 on. That did not happen. That drives directly to 20 the substance of the paper, methods and results.</p> <p>21 Q Well, did you run the meta-analysis, 22 leaving Booth out, to check whether it had any 23 effect on the results?</p> <p>24 A No. I wasn't -- I wasn't tasked with 25 trying to figure out how to do this the right way.</p> |

April Zambelli-Weiner, Ph.D.

| Page 267 | Page 269 |
|--|---|
| <p>1 That wasn't my job. 2 Q Well, did you run the analysis with 3 including the -- the lowest dose from Booth to see 4 if it had any effect on the results? 5 A Again, not my charge. Simply defending 6 the facts, as you asked me originally, that this 7 is a -- a substantive error. 8 Q If you look at the next point you make 9 over at the top of page 16, that's looking at the 10 Cook data. Do you see that? 11 A Yes. 12 Q And what they -- the authors did there 13 was to convert the -- 14 THE REPORTER: Was to what? 15 THE WITNESS: I'm sorry. 16 BY MR. HEGARTY: 17 Q And what the authors did there was to 18 convert the days reported to years, correct, 19 from -- from the Cook study? 20 A That -- that's what they attempted to 21 do, correct. 22 Q And your issue is with the fact that the 23 intervals overlap, correct? 24 A Correct. And also that the -- the 25 categories are rounded incorrectly if you -- if</p> | <p>1 this, you know, figure out how -- what the right 2 way to do it was. 3 Q Well, if the authors had used the 4 numbers you said they should have used, would it 5 have made -- had any effect on the risk numbers 6 that they reported or the conclusions from the 7 study? 8 A Can you repeat the question? 9 Q Sure. 10 If the authors had used the numbers from 11 Cook that you say they should have used, would it 12 have had any effect on the risk numbers they 13 reported or the conclusions from the study? 14 A Well, I think -- I think in this 15 particular case I'm -- I'm simply calling out the 16 misrepresentation of the -- of the exposure 17 categories. There may be other Cook-related 18 errors. But, again, standing -- standing by my -- 19 my position that it's paramount that the data be 20 accurately represented from the underlying 21 studies. 22 Q Well, what would the risk number have 23 been if they had used what you say is the accurate 24 data from Cook? 25 A I -- I can't answer that.</p> |
| <p style="text-align: center;">Page 268</p> <p>1 you extrapolate that. 2 Q Well, did you tell the reader of your 3 report what the numbers should have been listed 4 as? 5 A I don't know. I don't believe so. 6 Q Well, what was the substantive effect on 7 the results from the way they characterized the 8 data from Cook in terms of lifetime days? 9 A Again, anything that drives at the 10 methods and the results of the meta-analysis is a 11 substantive error. And I'm just going to bring it 12 right back to the foundation of a valid 13 meta-analysis, which is an analysis of someone 14 else's data, of someone else's study, and proper 15 representation of that data is paramount to the 16 foundation of a valid meta-analysis. 17 So, you know, inaccurately representing 18 the data from another study to me is a substantive 19 error. It drives directly at the analysis, the 20 methods and the results. 21 Q Well, did you run the meta-analysis 22 using what you believed were the proper numbers 23 from Cook? 24 A Again, I -- I was not charged with that. 25 It wasn't my -- wasn't my task or my job to rerun</p> | <p style="text-align: center;">Page 270</p> <p>1 Q Well, what would the conclusions have 2 been if they had used the accurate numbers from 3 Cook as you say they should have? 4 A Again, you know, this -- this is just 5 about the, you know, inaccurate, incorrect 6 representation of the data from the original 7 studies, and another example of this in the 8 context of a lot of other issues. 9 So I'm also -- also not entirely 10 comfortable -- I know -- I know you want to walk 11 through these one at a time, but they do each 12 exist within -- within a broader context of -- of 13 a lot of other issues. 14 Q The next point you make refers to the 15 data that they used from the Gertig study, in 16 particular leaving out the "never and less than 17 one week." Do you see where I'm referencing? 18 A Yes, I do. 19 Q Again, as with Booth, a never and 20 less-than-one-week level of exposure could not be 21 combined with the other data that they were 22 looking at for purposes of the meta-analysis, 23 correct? 24 A Well, again, that's your assertion and 25 your supposition about what the authors did. I --</p> |

April Zambelli-Weiner, Ph.D.

| Page 271 | Page 273 |
|---|---|
| <p>1 they don't tell us what they did. And -- well, 2 they do tell us what they did, and they didn't do 3 that, so they did something different than that, 4 which we don't know exactly what they did. 5 So, again, same answer as before: This 6 is just another example of, you know, 7 misrepresenting the data from the original 8 studies, leaving out exposure categories, without 9 proper explanation of exactly what they did and 10 exactly why they did it. 11 Q Well, do you intend to testify that the 12 authors intentionally misrepresented the data from 13 the original studies? 14 MR. TISI: Objection. 15 THE WITNESS: I can't speak to what 16 their intent was. But you can mislead -- it's 17 misleading, period. I don't know what their 18 intent was, but it's misleading. 19 BY MR. HEGARTY: 20 Q Well, is it your -- is it your testimony 21 that they tried to be misleading or they tried to 22 misrepresent the data? 23 A Again, I -- I can't say what their 24 intent was. I can simply say that there is 25 misleading data, there's misleading statements</p> | <p>1 MR. TISI: Objection. 2 THE WITNESS: Well, I wouldn't agree 3 with that. Again, I'm going to come back to the 4 foundation of what a meta-analysis is. And I do 5 believe, again, the authors state somewhere in 6 their paper -- hopefully I'm again recalling 7 correctly -- yes, two researchers performed the 8 data abstraction. 9 So this raises a lot of questions for me 10 as a researcher when I see these kinds of errors, 11 because you have to understand in a meta-analysis, 12 you're really talking about, like, copy and paste. 13 I mean this is just -- you're not running 14 calculations with regard to the abstraction of the 15 data. You're literally copying and pasting from 16 another person's study to, you know, your data 17 abstraction form. 18 So, to have these kinds of errors under 19 the assertion that there was a double abstraction 20 process raises a lot of questions for me, and I 21 would think for any researcher, because how is it 22 that two people independently abstract the same 23 error incorrectly? 24 BY MR. HEGARTY: 25 Q Well, what would have been the effect on</p> |
| <p>1 throughout their works. That's just a fact. 2 Q Well, what would have been the numbers 3 reported from the study if they had included the 4 lowest dosage category from Gertig? 5 A I can't answer that, because a whole 6 dose-response methodology should be laid out. 7 It -- there's many different ways to come at this. 8 They didn't do that, so I can't evaluate that. 9 It's really a hypothetical. 10 Q If you look at the next point you make, 11 it's the third cell in the carryover table on 12 page 16, it concerns the odds ratio and confidence 13 interval reported from the Chang study, correct? 14 A I'm sorry, are you third from the 15 bottom? 16 Q No, the third cell down from the top. 17 A Okay. Same. 18 Q Same. 19 A Okay. 20 Q You're talking there about the odds 21 ratio in one instance and the confidence interval 22 in another instance from the Chang study, correct? 23 A Correct. 24 Q Those are likely typographical errors, 25 correct?</p> | <p>1 the risk numbers reported if they had used the 2 proper odds ratio and confidence interval, as you 3 say they should have? 4 A Again, that -- that wasn't my charge. 5 That wasn't my task. I'm simply laying out that 6 they did not abstract the data from the underlying 7 studies correctly. 8 And in some cases -- you know, you have 9 to understand how meta-analysis works. These 10 errors are substantive to the results of the 11 meta-analysis. I can't speak to what the direct 12 specific impact of that would be because I wasn't 13 tasked with designing this meta-analysis, and -- 14 and making those methodologic judgments myself and 15 going through that process. 16 But I can tell you that a valid 17 meta-analysis is based on the foundation of 18 accurate and meticulous abstraction of the data 19 from the original studies. And so if that is not 20 done, that is in fact a substantive error. 21 Q Well, what was the substantive impact of 22 having a confidence interval of 1.09 to 2.68 23 versus 1.09 to 2.64? 24 A Again, I can't tell you specifically. 25 All I can tell you is that even small errors can</p> |

April Zambelli-Weiner, Ph.D.

| Page 275 | Page 277 |
|---|---|
| <p>1 become amplified in a meta-analysis. So I can 2 just talk qualitatively about what can happen. 3 Rounding errors, these kinds of errors, they can 4 have impact on the results because you are 5 weighting these studies, and so depending upon how 6 the studies get weighted, errors get -- can become 7 amplified. It is absolutely core to the substance 8 of a meta-analysis.</p> <p>9 Q Is it your testimony that a 2.68 versus 10 a 2.64 higher confidence interval in that one cite 11 would have caused substantive error in the risk 12 numbers that were calculated?</p> <p>13 A Again, I'm going to stand by my prior 14 testimony that I'm not -- I'm not -- first of all, 15 I wasn't charged with doing that.</p> <p>16 Second of all, do I think that that one 17 little like 0.04 is going to have by itself a 18 major impact on the results? Probably not. Is it 19 still a substantive error? Yes, it is. And does 20 it exist within the context of a lot of other 21 errors that compounded and together can have a 22 substantive impact on the results? Yes, it 23 absolutely does.</p> <p>24 Q In the next cell, you again cite a 25 confidence interval that was cited as 0.6 to 3.4</p> | <p>1 if they had used in the -- the next part 2.4 2 instead of 3.4?</p> <p>3 A I would say it's -- it's again the same 4 answer. It just shouldn't happen.</p> <p>5 Q The next point you make is that the Ness 6 reference included use on feet, correct?</p> <p>7 A Correct.</p> <p>8 Q The number listed, though, was from the 9 Ness paper, and those -- that number are for 10 genital and rectal use and feet, correct?</p> <p>11 A Can we pull up the paper?</p> <p>12 Q Sure. You have it in front of you, 13 right?</p> <p>14 A Yeah.</p> <p>15 Q And for the record, I will mark that 16 paper as Exhibit 17. (Exhibit No. 17 was marked for identification.)</p> <p>19 BY MR. HEGARTY:</p> <p>20 Q In particular, if you turn over to 21 Table 2 of Exhibit 17, on page 114 -- are you 22 there with me, Doctor?</p> <p>23 A I am. I'm sorry. Yes, I'm there.</p> <p>24 Q And you see that the numbers that the 25 2003 article reported were for talc use,</p> |
| <p style="text-align: center;">Page 276</p> <p>1 when it should have been 0.6 to 2.4. Do you see 2 where I'm reading?</p> <p>3 A I do, yes.</p> <p>4 Q What was the substantive impact to the 5 results of this paper by having a confidence 6 interval of -- of 0.6 to 3.4 instead of 0.6 to 7 2.4?</p> <p>8 A I would say, again, it's -- it's the 9 same answer. And, you know, we didn't really talk 10 about the one above it either, which is -- which 11 is pretty substantive to misrepresent the point 12 estimate in Chang, so just bringing that to -- to 13 the forefront as well.</p> <p>14 So, I mean, you know, again, it's -- 15 it's -- one, it's a substantive error; and, two, 16 they exist within the context of -- of a lot of 17 errors. And so I can't answer what the specific 18 impact would be of the accumulation of these -- of 19 these substantive errors.</p> <p>20 Q Well, going back to the -- to the Chang 21 reference, what would have been the numbers 22 reported if they had used 0.865 instead of 0.96?</p> <p>23 A I can't answer that, and quite frankly, 24 we shouldn't have to wonder.</p> <p>25 Q Well, what would have been the numbers</p> | <p style="text-align: center;">Page 278</p> <p>1 genital/rectal and feet, correct?</p> <p>2 A That is correct.</p> <p>3 Q So it wasn't just limited to feet, as 4 you say in your report, correct?</p> <p>5 A Well, it does include feet, and if you 6 look at the section above on talc use, you can see 7 that a large proportion of the talc exposure was 8 feet. And I think that this is really important 9 as it relates to the author's stated objectives of 10 this paper, which if I'm recalling correctly, are 11 perineal cosmetic talc use.</p> <p>12 And so I think that that is an important 13 limitation or aspect of this data that is 14 questionable in terms of whether this should 15 have -- would have even met the inclusion/ 16 exclusion criteria if that had been clearly 17 specified. Whether that drives at the -- at the 18 research question, which is -- which really gets 19 to validity.</p> <p>20 I mean validity is, are you measuring 21 what you say you're measuring. So if you're 22 measuring perineal talc -- if you're saying you're 23 measuring perineal talc, but you're actually 24 measuring feet also, that's an issue.</p> <p>25 Q Doctor, the category they used are for</p> |

April Zambelli-Weiner, Ph.D.

| Page 279 | Page 281 |
|--|--|
| <p>1 genital/rectal use, and feet. So every person in 2 the list -- every person from the dataset that 3 they used used talc on the genitals and rectal 4 area, correct?</p> <p>5 A It says "genital/rectal and feet." 6 That's what it says, correct.</p> <p>7 Q So it did not include just users on 8 their feet, correct?</p> <p>9 MR. TISI: Objection.</p> <p>10 THE WITNESS: I don't -- I don't know 11 that I necessarily agree with that. I mean if you 12 look above, you know, the genital/rectal use is 13 161 cases. There's clearly more than 161 cases 14 represented in -- in that section.</p> <p>15 So, you know, regardless, it's very 16 possible that it includes people who only had foot 17 exposure, and at a minimum, I think this is an 18 important substantive issue.</p> <p>19 BY MR. HEGARTY:</p> <p>20 Q You say it's very possible that the 21 category that Dr. Ness reported on in Table 2 22 included cases and controls who only used it on -- 23 on feet? Is that what you're saying?</p> <p>24 A Well, I need to look a little more 25 closely.</p> | <p>1 that can include people with feet exposure, not 2 genital/rectal.</p> <p>3 BY MR. HEGARTY:</p> <p>4 Q Okay. Your next point as we were 5 walking through Table 1 on pages 15, 16, 17 of 6 your report, we're looking at the top of page 17, 7 you make reference to misstating the year of a 8 publication.</p> <p>9 How is that a substantive error?</p> <p>10 A Again, this -- this I cite here because 11 it's an important methods reference. So, again, 12 my definition of "substantive," anything that 13 drives at the methods or the -- you know, the 14 results of the -- of the study.</p> <p>15 Q Misstating the year would not have had 16 any substantive effect on the numbers that the 17 authors ran, would -- would it?</p> <p>18 MR. TISI: Objection.</p> <p>19 THE WITNESS: No, I think -- sorry.</p> <p>20 MR. TISI: I'm sorry.</p> <p>21 Objection. Misstates, asked and 22 answered.</p> <p>23 BY MR. HEGARTY:</p> <p>24 Q You -- you can answer.</p> <p>25 A Okay, sure. Yeah, I think this -- this</p> |
| Page 280 | Page 282 |
| <p>1 MR. TISI: Excuse me. Could we go off 2 the record? I'm so sorry.</p> <p>3 MR. HEGARTY: Okay. Let's go off the 4 record.</p> <p>5 THE VIDEOGRAPHER: The time is 6 11:01 a.m., and we're going off the record. 7 (Recess.)</p> <p>8 THE VIDEOGRAPHER: The time is 9 11:11 a.m., and we're back on the record.</p> <p>10 BY MR. HEGARTY:</p> <p>11 Q Doctor, when we broke we were talking 12 about the reference to the Ness paper and 13 including the category of genital/rectal and feet, 14 and I asked you to let me know whether you thought 15 that that category did -- did or would have 16 included individuals who did not also use talc on 17 the genital/rectal area.</p> <p>18 A Correct.</p> <p>19 Q Is that still your testimony?</p> <p>20 A Yes. After reviewing the paper -- well, 21 let's just say after reviewing Table 2 but not 22 rereviewing the entire paper --</p> <p>23 MR. TISI: Table 2 of the Ness paper.</p> <p>24 THE WITNESS: I'm sorry. Table 2 of the 25 Ness paper, it is my interpretation of that, that</p> | <p>1 would drive more at the methods of the study.</p> <p>2 Q Also, the next point you make about the 3 text referring to seven studies but the -- the 4 table including only six studies, how would that 5 have had an effect on the numbers that the study 6 reported?</p> <p>7 A I think this goes back to what we were 8 talking about before in that the dose-response 9 analysis leaves a lot of -- of questions as to 10 what was actually done. And so I think with all 11 of that in mind, again, the contradiction is open, 12 but -- because we don't have an adequate 13 description of the methods, we have 14 contradictions, and we don't have the reporting 15 out of the meta-analysis showing us, you know, 16 exactly what went into the meta-analysis.</p> <p>17 Q Your last point refers to the rounding 18 of numbers. Rounding of numbers in doing a 19 meta-analysis is not, per se, improper, correct?</p> <p>20 A I would say I don't necessarily agree 21 with you, with a caveat. You know, meta-analysis 22 really is about representing the data from the 23 original studies. If there's a reason to round 24 numbers, if that's a methodologic choice that was 25 made by the investigators, then I would hope that,</p> |

April Zambelli-Weiner, Ph.D.

| Page 283 | Page 285 |
|---|--|
| <p>1 one, they would describe that choice; and, two, 2 justify that choice; and, three, apply it 3 uniformly. 4 So this -- and this does speak to the 5 point that I made before, which is, you know, 6 those types of rounding errors can have a 7 substantive impact on the results, particularly as 8 it relates to the weights and how much weight a 9 particular study gets. So I think that is 10 absolutely a substantive error. 11 Q Did you do an analysis comparing what 12 the results would have been if they had not 13 rounded versus the results because they did round? 14 A Again, same answer as -- as before, no, 15 that wasn't my -- my charge. 16 Q The results from this meta-analysis, 17 that is, the 2003, the relative risk -- or I 18 should say the odds number reported of 1.23 is 19 comparable to the other meta-analysis that had 20 been done, correct? 21 A I'm sorry. Are we -- are we -- so we're 22 back on the main meta-analysis? 23 Q We're on the 2003 meta-analysis. 24 MR. TISI: He shifted from the -- the 25 dose-response.</p> | <p>1 BY MR. HEGARTY: 2 Q If you look at the section on page 18 3 entitled "Lack of replication, 2003 Huncharek 4 meta-analysis." Do you see where I am? 5 A Yes. 6 Q Your first sentence says: "In their 7 2003 paper, Drs. Huncharek and Muscat claim that 8 their calculations suggest an inverse dose 9 repose." 10 That's wrong, isn't it? 11 A There's a missing S, correct. 12 Q That's a mistake in your report, right? 13 A That's a -- that's a typo, yes, correct. 14 Q Does that make your report 15 substantively -- should be questioned 16 substantively? 17 A Well, I think I did, one, further make 18 that distinction, but, two, also reiterate that 19 it's the totality of the errors in any particular 20 piece of work. 21 Q But your quality control did not pick up 22 that error, correct? 23 A That is correct, yes. 24 Q Is it your contention that as of 2003, 25 it was wrong to say that the dose-response numbers</p> |
| Page 284 | Page 286 |
| <p>1 THE WITNESS: Okay. 2 BY MR. HEGARTY: 3 Q The numbers they report for the relative 4 risks of their meta-analysis of 1.23 are 5 comparable to all of the other meta-analysis that 6 had been conducted at that point in time and that 7 have been conducted since, correct? 8 A I can't really answer that. I wasn't 9 charged with doing that analysis, so I -- it 10 wouldn't be fair for me to speculate. 11 Q But you had not -- you did not go back 12 and look at the other meta-analysis to see if the 13 numbers that the 2003 paper reported are 14 consistent with what other meta-analyses have 15 reported? 16 A Again, no, I didn't do an exhaustive 17 review of all the meta-analyses. No. 18 Q So can you testify that the -- the 19 numbers they reported from this study are 20 different than all the other meta-analysis that 21 have been done in a substantive way? 22 MR. TISI: Objection. 23 THE WITNESS: Again, not -- not my 24 charge. Didn't do that analysis, so wouldn't want 25 to comment on it.</p> | <p>1 available suggested an inverse dose-response 2 relationship? 3 A I'm not sure I understand your question. 4 Can you rephrase or be specific? 5 Q Was it your contention that as of 2003, 6 it was wrong to say that the dose-response data 7 from the talc ovarian cancer studies argued 8 against a causal relationship? 9 MR. TISI: Can you see -- you don't have 10 a -- let me give this to you because that may be 11 easier if you want to -- 12 THE WITNESS: So if I'm understanding 13 you correctly, you're asking me to make an 14 assessment about the body of evidence as a whole 15 related to dose-response? 16 BY MR. HEGARTY: 17 Q Well, let me ask it differently. 18 Are you contending that it was wrong for 19 the 2003 paper to -- to say that the dose-response 20 data available suggested an inverse dose-response? 21 A I think that what I'm saying is that 22 there are validity issues with the dose-response 23 analysis as presented in that paper that, yes, 24 bring me to the conclusion that that is not a 25 valid analysis, and that therefore is not a valid</p> |

April Zambelli-Weiner, Ph.D.

| Page 287 | Page 289 |
|---|---|
| <p>1 conclusion from that analysis. 2 Q Well, the authors actually note in their 3 paper that they had limitations on what they could 4 do in terms of calculating dose-response, over on 5 page 1958, correct? 6 A Do you want to point me to -- 7 Q Yeah, in the third -- the paragraph in 8 the middle, they say -- after saying, "These data 9 suggest an inverse relationship between talc 10 exposure and ovarian cancer risk. Unfortunately, 11 only limited data were available." Do you see 12 that section? 13 A Yes. 14 Q So they describe the limitations that 15 they had in terms of analyzing dose-response, 16 correct? 17 MR. TISI: Objection. 18 THE WITNESS: They do discuss some 19 limitations of -- of the analysis. That doesn't 20 necessarily mean they address all of the issues 21 that I brought up. 22 BY MR. HEGARTY: 23 Q Well, it's not improper to include 24 limitations in terms of what's available for an 25 analysis in an article, correct?</p> | <p>1 mixed exposure category. Correct? 2 A Correct. 3 Q You note that the studies included nine 4 studies, correct? 5 A Correct. 6 Q But nowhere in your report do you list 7 what those nine studies were, correct? 8 A I don't know if that's true, but I do 9 believe I reference Table 2, which is where the 10 nine studies are. Table 2 in the 2003 Huncharek 11 paper. 12 Q So the nine studies you're making 13 reference to in that part of your report refers to 14 Table 2 in the 2003 study. 15 A Yes, I believe so, and that's what's in 16 the methods summary below. 17 Q As to your calculations, again, you're 18 reporting here what was done in the 2003 paper 19 we've been looking at, correct? 20 A Well, what I'm reporting here is my 21 attempt to replicate the two summary risk 22 estimates that are reported for the, 23 quote/unquote, lowest exposure cat- -- reported 24 exposure category and the highest exposure 25 category in the 2003 paper.</p> |
| <p>1 MR. TISI: Objection. 2 THE WITNESS: No, I -- it's not 3 improper. I mean, I think it's -- it's something 4 that's expected to discuss limitations, but I 5 think now we're shifting from one thing, which is 6 the validity of the analysis, to what the authors 7 discuss in their Discussion section. 8 BY MR. HEGARTY: 9 Q Well, did you do an independent analysis 10 of the dose-response data available as of 2003 to 11 determine whether it did suggest an inverse 12 dose-response? 13 A Well, what I did, which is in my report, 14 is try to replicate their dose-response analysis. 15 I did not do necessarily a broader evaluation of 16 the entire evidence base with regard to 17 dose-response. That was not -- that was not my 18 charge. 19 Q Well, if we turn over to page 20 of your 20 report, where you do what you say you just did of 21 trying to replicate what the authors did, you 22 report that -- the data that you generated in 23 Table 2, correct? 24 A Correct. 25 Q One of the categories that you use is a</p> | <p>1 Again, because we don't -- we have lots 2 of questions about what actually was done, we have 3 a lack of description of the methods, and we don't 4 have the reporting out of the results, as we 5 discussed previously. So there's a question as to 6 what was actually done and how they actually 7 arrived at those particular sum- -- summary risk 8 estimates. 9 So what I'm doing here is trying to 10 figure that out, given all of those gaps, and 11 trying to take what they said they did, the 12 references they cited, and a standard generally 13 accepted approach to meta-analysis to see if we 14 can arrive at the same answers. 15 Q Well, the first column, you report on 16 the Huncharek and Muscat method, correct? 17 A Correct. 18 Q Again, Dr. Muscat was not an author on 19 the 2003 paper, correct? 20 MR. TISI: Objection. Asked and 21 answered. 22 THE WITNESS: I think we -- I think we 23 talked about that, you know, my -- excuse me, my 24 reference to him in terms of his involvement and 25 the fact that this dose-response data actually</p> |

April Zambelli-Weiner, Ph.D.

| Page 291 | Page 293 |
|--|--|
| <p>1 derives from a much earlier report. 2 BY MR. HEGARTY: 3 Q Well, can you cite for me any authority 4 to say that Dr. Muscat was in any way involved in 5 the publication of the 2003 meta-analysis? 6 A Again, I think -- I think I answered 7 that. I'm -- I'm referring back to the original 8 proposal, preliminary data reports, and possibly 9 his -- his deposition, with the caveat that I 10 obviously don't remember every word of his 11 deposition. 12 Q Okay. The authors in the 2003 paper did 13 identify the methods they used to do the 14 meta-analysis, correct, in the methods -- in the 15 materials and methods section, correct? 16 MR. TISI: Dose-response or the overall, 17 Counsel? 18 MR. HEGARTY: I'm referring to this 19 table. 20 MR. TISI: Okay. 21 BY MR. HEGARTY: 22 Q In the materials section, they described 23 the methods they used as a general, variance-based 24 method employing confidence intervals, correct? 25 A Correct. So they -- they do two things.</p> | <p>1 Q Correct. 2 A Okay. And I'm looking. 3 I would say that appears to be correct 4 with -- you know, with the context of, first of 5 all, none of these match exactly to what's 6 reported in the paper. And, two, it should be 7 noted that there's significant overlap of the 8 confidence intervals across this table, which is 9 an important methodologic -- or result, I should 10 say, in terms of how you interpret these findings. 11 Q But the adjusted numbers you're 12 reporting show an inverted dose-response, correct? 13 MR. TISI: Objection. 14 THE WITNESS: I would not characterize 15 it that way. I would not characterize it -- I 16 certainly would not put this data forward as 17 strong evidence of an inverse dose-response. That 18 is not something I would do. 19 BY MR. HEGARTY: 20 Q You do agree, though, that the higher -- 21 the lowest exposures in all cases had a higher 22 point estimate than the higher exposures for the 23 adjusted numbers, correct? 24 MR. TISI: Objection. 25 THE WITNESS: Again, and -- so that --</p> |
| Page 292 | Page 294 |
| <p>1 They say the data analysis was performed according 2 to Greenland, and they cite Greenland, and then 3 they also list a series of equations there. And 4 so there is some discrepancy between the equations 5 listed here and what is in Greenland. 6 And so, again, not knowing what exactly 7 was done, we ran it -- you know, I ran it both 8 with the formulas as reported and then with the 9 formulas from Greenland. 10 Q As for -- excuse me -- as for your 11 calculations, which are the Greenland method and 12 the fixed -- actually, you did all three, correct? 13 A Correct. 14 Q As to all three calculations that you 15 did by every method, the odds ratio for the 16 adjusted lowest category of dose is higher than 17 the odds ratio for the highest category of dose, 18 correct? 19 A I'm sorry. Let me read that back. 20 (Reading monitor.) 21 Okay. So if I'm understanding you 22 correctly, you're asking if the reported point 23 estimates are higher for -- across the board for 24 the adjusted lowest exposure category compared to 25 the highest exposure category.</p> | <p>1 that is correct, you are reading the table 2 correctly. 3 But again, to go back, I think we need 4 to just revisit the premise of there's incorrect 5 data here. I don't agree with the premise of the 6 -- the methodologic choice of the authors related 7 to the dose-response analysis. So taking the 8 authors' data in Table 2 at face value, we are 9 unable to replicate the numbers in their study. 10 But, you know, to bring it back to 11 answer your question, yes, you are -- you are 12 reading that correctly. 13 BY MR. HEGARTY: 14 Q But you're replicating their commentary 15 that the data suggests an inverse dose-response, 16 correct? 17 MR. TISI: Objection. 18 THE WITNESS: Again, I would not 19 interpret this data in that way. There's 20 significant overlap of the confidence intervals. 21 This in no way -- and again, this is based on 22 incorrect data and in a -- in a flawed analysis. 23 So just stopping at those first two points, I 24 would never do this analysis. This is not an 25 analysis I would do. And so I can't validate it.</p> |

April Zambelli-Weiner, Ph.D.

| Page 295 | Page 297 |
|---|--|
| <p>1 I wouldn't put it forward in that way. 2 But just taking the fact that they did 3 do that and there are errors in the data, that 4 even with these results, I would not put this 5 forward as strong evidence of -- of an inverse 6 dose-response. I would not use this to support 7 that point.</p> <p>8 BY MR. HEGARTY:</p> <p>9 Q Doctor, if you look over on page 19 of 10 your report, in the last paragraph marked 3, you 11 actually say that the data you ran suggests a 12 positive dose-response. So you're taking your 13 data and saying it suggests a positive 14 dose-response, correct?</p> <p>15 A I'm not -- no. I -- I make a 16 distinction here. I'm simply reporting on the 17 finding, just as I just conceded to you that in 18 fact that's what the data says.</p> <p>19 What I'm saying is in fact when you run 20 it with -- with standard generally accepted 21 statistical packages, you actually see a different 22 trend. That's very different than putting this 23 data forward and advocating it in -- in support of 24 a very important, you know, aspect regarding a 25 causal -- a causal question.</p> | <p>1 A Well, that's a very -- that's a 2 different question. That's a very broad question. 3 I mean, it depends on -- you know, I wasn't 4 designing this analysis. That's very different. 5 If I'm going to design an analysis, I'm going to 6 go through the process of evaluating confounding 7 and deciding whether unadjusted or adjusted 8 numbers are the right way to go. 9 This was done in response to 10 Dr. Muscat's deposition in which he alluded to the 11 fact that unadjusted numbers may have been used in 12 the meta-analysis. So just to cover all possible 13 permutations, that's why unadjusted values are 14 included here.</p> <p>15 Q Well, you say in that paragraph that 16 with the adjusted data for the number of talc 17 applications per month actually showing a data -- 18 showing data suggesting a positive dose-response. 19 What adjusted data from the number of 20 application -- talc applications per month -- 21 MR. TISI: Show her where she says -- 22 BY MR. HEGARTY: 23 Q -- suggest a positive dose-response? 24 MR. TISI: Where is -- where are you 25 referring to, Counsel?</p> |
| <p>1 So I will agree with you that I'm making 2 that observation that in certain cases it does 3 flip, the trend flips, and that's an interesting 4 finding. But I'm not putting -- I'm not now 5 taking this result and disseminating it to FDA or 6 to the -- to the medical and scientific community 7 and saying, Look, this is proof of a positive 8 dose-response. That's an important distinction.</p> <p>9 Q Well, what data points suggest a 10 positive dose-response?</p> <p>11 A Again, there are certain instances where 12 the point estimates increase. Just as you 13 indicated there are situations where they 14 decrease, there are scenarios in this table where 15 the point estimate increases from the lowest to 16 the highest exposure at that point.</p> <p>17 Q Just tell me which point estimates 18 suggest a positive dose-response.</p> <p>19 A The unadjusted applications per month. 20 Again, with the caveat of the description that 21 I've just provided.</p> <p>22 Q So it's your testimony that it's proper 23 to look at unadjusted numbers rather than adjusted 24 numbers to say that there's a suggestion of a 25 dose-response?</p> | <p>1 MR. HEGARTY: If you follow along, I was 2 at the page -- bottom of page 9. 3 MR. TISI: Well, she is looking for it 4 too. Bottom of page -- you're not going to tell 5 me?</p> <p>6 MR. HEGARTY: 19. 7 MR. TISI: Thank you. 8 THE WITNESS: Oh, I see what you're 9 saying. I see what you're saying. I think that 10 should say unadjusted.</p> <p>11 BY MR. HEGARTY: 12 Q So that's another mistake in your 13 report?</p> <p>14 A I'm just checking. (Peruses document.) 15 I think that's correct, I think it 16 should say "unadjusted."</p> <p>17 Q Okay. Over on page 21 of your report, 18 in the third paragraph beginning "In his 19 deposition" -- do you see where I'm reading? 20 A Yes. 21 Q You again note that: "The results for 22 frequency per month" -- this is at the end of the 23 paragraph -- "measure change appreciably, 24 including demonstrating increasing risk with 25 increasing exposure for the analysis using talc</p> |

April Zambelli-Weiner, Ph.D.

| Page 299 | Page 301 |
|--|---|
| <p>1 applications per month."</p> <p>2 So is it your testimony that the numbers</p> <p>3 you generated demonstrate increasing risk with</p> <p>4 increasing exposure for talc applications per</p> <p>5 month?</p> <p>6 A I think I just -- I think I just</p> <p>7 answered that before. Again, juxtaposing to</p> <p>8 the -- the data -- first of all, the data that</p> <p>9 they report in their -- in their study, which, by</p> <p>10 the way, is again not resemble indicated here.</p> <p>11 I'm simply making the observation that there is a</p> <p>12 reversing of that trend. And, you know, it's an</p> <p>13 interesting finding that using standard accepted</p> <p>14 statistical packages for meta-analysis, which one</p> <p>15 must wonder why they weren't used in the first</p> <p>16 place, that that does result in a different trend</p> <p>17 in terms of dose-response. So if someone was</p> <p>18 going to take these data and use them in that way,</p> <p>19 that that trend is in fact reversed.</p> <p>20 Q The adjusted numbers don't show that, do</p> <p>21 they?</p> <p>22 A I think we just -- I think we just</p> <p>23 covered that. I believe it's the unadjusted, yes.</p> <p>24 Q So are you saying it's proper in a paper</p> <p>25 to choose an unadjusted number to say it</p> | <p>1 Is there a risk of bias due to residual</p> <p>2 confounding? So that has to be -- that's a</p> <p>3 methodologic decision that involves, you know,</p> <p>4 expert analysis, expert judgment, and in some</p> <p>5 cases confounding is not a concern, and therefore</p> <p>6 the unadjusted may in fact be the appropriate</p> <p>7 number to use.</p> <p>8 Q Is that the appropriate number to use</p> <p>9 here?</p> <p>10 MR. TISI: Objection.</p> <p>11 THE WITNESS: Again, that wasn't my</p> <p>12 charge or my process. So I'm -- I -- I can't</p> <p>13 answer that. I told you why I was including that,</p> <p>14 and that's all I can say about it.</p> <p>15 BY MR. HEGARTY:</p> <p>16 Q Did you do a trend analysis to try to</p> <p>17 show dose-response?</p> <p>18 A No. Again, I was simply trying to</p> <p>19 replicate. I was not doing an independent</p> <p>20 dose-response analysis.</p> <p>21 Q When you're doing a fixed effects</p> <p>22 analysis, is it proper to combine relative risk</p> <p>23 with odd ratio -- odds ratios?</p> <p>24 A Sure. I mean, there are certain times</p> <p>25 where that would -- that would be appropriate. I</p> |
| <p>1 demonstrates increasing risk with dose versus the</p> <p>2 adjusted number which doesn't?</p> <p>3 A Again, I think you're asking me an</p> <p>4 abstract question. I explained why I included</p> <p>5 unadjusted here in this analysis. If I was going</p> <p>6 to go about doing an analysis that I was going to</p> <p>7 put forward and -- and advocate for or publish, I</p> <p>8 would go through that process of deciding.</p> <p>9 That was not my charge here. That was</p> <p>10 not the process, and I've only -- you know, I've</p> <p>11 included unadjusted, as I said, because Dr. Muscat</p> <p>12 offered that perhaps that -- that describes or</p> <p>13 explains some of the discrepancies that we were</p> <p>14 seeing.</p> <p>15 Q Well, in an article of yours, have</p> <p>16 you -- when you've had both an adjusted and an</p> <p>17 unadjusted number, have you ever gone with the</p> <p>18 unadjusted number versus the adjusted number?</p> <p>19 A Sure. Yes.</p> <p>20 Q So you -- it's proper methodology when</p> <p>21 you have an adjusted number and an unadjusted</p> <p>22 number to go with the unadjusted number?</p> <p>23 A Well, it's a contextual question that</p> <p>24 involves that research question and that data. I</p> <p>25 mean, it's a question of is confounding an issue.</p> | <p>1 mean, when the outcome is rare, the odds ratio</p> <p>2 approximates the relative risk.</p> <p>3 Q How about if the outcome is not rare.</p> <p>4 Is it proper to combine relative risk numbers with</p> <p>5 odds ratio numbers in doing a fixed effect</p> <p>6 analysis?</p> <p>7 A I think I'd have to review the question</p> <p>8 and review the studies, and -- and make that</p> <p>9 judgment.</p> <p>10 Q Over on page 21 under -- before Part 3,</p> <p>11 do you see the paragraph before -- before Part 3?</p> <p>12 A Yes.</p> <p>13 Q You make reference again to this data</p> <p>14 was asserted to the FDA in 2009. Do you see where</p> <p>15 I'm reading?</p> <p>16 A Yes.</p> <p>17 Q The FDA did not report in their 2014</p> <p>18 denial letter that there was an inverse</p> <p>19 dose-response, did they?</p> <p>20 A I don't recall exactly what they -- what</p> <p>21 they say.</p> <p>22 MR. TISI: Here you go. Don't worry</p> <p>23 about that.</p> <p>24 THE WITNESS: Okay.</p> <p>25 BY MR. HEGARTY:</p> |

April Zambelli-Weiner, Ph.D.

| Page 303 | Page 305 |
|---|--|
| <p>1 Q Do you have Exhibit 12 there?</p> <p>2 MR. TISI: Oh, this is --</p> <p>3 MR. HEGARTY: Did you find it?</p> <p>4 MR. TISI: I'm looking for it.</p> <p>5 MR. HEGARTY: It wouldn't be the last</p> <p>6 exhibit.</p> <p>7 MR. TISI: Yeah, it wasn't. That's why</p> <p>8 I'm looking for it.</p> <p>9 THE WITNESS: Can I just take a quick</p> <p>10 break after -- after this question?</p> <p>11 MR. HEGARTY: Well, let's take a quick</p> <p>12 break now so you can -- let's go off the record.</p> <p>13 THE WITNESS: Okay. Thanks.</p> <p>14 THE VIDEOGRAPHER: The time is 11:36</p> <p>15 a.m. We're going off the record.</p> <p>16 (Recess.)</p> <p>17 THE VIDEOGRAPHER: The time is 11:40</p> <p>18 a.m., and we're back on the record.</p> <p>19 BY MR. HEGARTY:</p> <p>20 Q Doctor, when we left off, I was going to</p> <p>21 ask you about the -- the 2014 letter, but I want</p> <p>22 to move on, so I'm not going to ask you questions</p> <p>23 about that.</p> <p>24 A Okay.</p> <p>25 Q I want to next move to page 22 of your</p> | <p>1 the plausible role of uncontrolled confounding in</p> <p>2 their analysis or the larger evidence base."</p> <p>3 Correct?</p> <p>4 A Correct. You read that correctly.</p> <p>5 Q But if you look at pages 956 -- I'm</p> <p>6 sorry, 958 and 959 of the study, the 2003 study --</p> <p>7 A 958 -- 1958.</p> <p>8 Q At the very bottom of 958, carrying over</p> <p>9 to 959, there they are analyzing whether weight,</p> <p>10 body mass index is a potential confounding factor,</p> <p>11 correct?</p> <p>12 A So, I'm sorry, just let me take a moment</p> <p>13 to look at this. (Peruses document.)</p> <p>14 So I think -- I think that this</p> <p>15 definitely is a very general discussion of some of</p> <p>16 the -- you know, they say a number of factors are</p> <p>17 known to influence ovarian cancer risk either</p> <p>18 positively or negatively.</p> <p>19 I'm just looking to see if this is part</p> <p>20 of the discussion section, but -- no, it looks</p> <p>21 like it's part of -- part of the results.</p> <p>22 But that is not to me a substantive</p> <p>23 discussion of -- or a substantive dealing of</p> <p>24 confounding as it relates to, you know, this</p> <p>25 particular research question.</p> |
| <p style="text-align: center;">Page 304</p> <p>1 report, the section entitled "Unsupported Claims</p> <p>2 of Bias from Uncontrolled Confounding."</p> <p>3 Do you see that page?</p> <p>4 A Page 22. Yes.</p> <p>5 Q The first italicized paragraph says:</p> <p>6 "Uncontrolled confounding may result in a spurious</p> <p>7 positive association between talc and ovarian</p> <p>8 cancer."</p> <p>9 That's a true statement, correct?</p> <p>10 A It depends if you're asking me like</p> <p>11 hypothetically or if you're asking me</p> <p>12 specifically.</p> <p>13 Q Just as a general proposition.</p> <p>14 A I would say, as a general proposition,</p> <p>15 uncontrolled confounding is a risk of bias to any</p> <p>16 epidemiologic study.</p> <p>17 With regard to the talc and ovarian</p> <p>18 literature, I wasn't tasked with doing that</p> <p>19 analysis, so I really can't offer an opinion as to</p> <p>20 whether I think uncontrolled confounding is an</p> <p>21 issue.</p> <p>22 Q Fair enough.</p> <p>23 At the bottom of page 22, you make</p> <p>24 reference to the study and say: "The authors</p> <p>25 provided no substantive evidence or discussion of</p> | <p style="text-align: center;">Page 306</p> <p>1 Q But they do -- and they are assessing</p> <p>2 there whether there's an effect of confounding on</p> <p>3 their result -- correct? -- in particular, on --</p> <p>4 with regard to weight and body mass index,</p> <p>5 correct?</p> <p>6 A If you want me to read this section,</p> <p>7 I'll read it.</p> <p>8 Q Well, I guess the -- you make the next</p> <p>9 statement in your report that says: "Based upon</p> <p>10 their description of their methods, it appears</p> <p>11 they do not evaluate and/or discuss what the</p> <p>12 important confounders are to the talc ovarian</p> <p>13 cancer research question."</p> <p>14 But in the part of the study I'm</p> <p>15 referring to, they do talk about weight, body mass</p> <p>16 index as a confounder, correct?</p> <p>17 A Well, again, I'm going to make a</p> <p>18 distinction between -- you know, with the caveat</p> <p>19 that I haven't read this -- this section and all</p> <p>20 the context around it, yeah.</p> <p>21 But what I can say is when you're doing</p> <p>22 a meta-analysis or when you're doing an epi study,</p> <p>23 the consideration of confounding really happens up</p> <p>24 front. And the point that I'm making here is</p> <p>25 there's no consideration of -- in a detailed way</p> |

April Zambelli-Weiner, Ph.D.

| | |
|--|--|
| <p style="text-align: center;">Page 307</p> <p>1 that informs the methods of what they consider to 2 be the important confounders to this relationship 3 because -- to this particular research question, 4 because that would obviously inform the methods of 5 the meta-analysis. 6 They don't make any distinction in the 7 meta-analysis methods that we're aware of saying, 8 Well, you know, studies must have adjusted for 9 these factors, because these are strong, important 10 confounders in the relationship. In fact, they 11 don't address it directly at all. 12 And when you actually get into the 13 tables of their paper, you actually see that there 14 are misrepresentations and sort of selective 15 choosing of risk estimates, some of which are only 16 age adjusted, when there are more fully adjusted 17 risk estimates. So it really begs a lot of 18 questions, again, as to what the authors' position 19 on confounding really was at the beginning of 20 this -- of this study and analysis, and it appears 21 to not have informed the analysis in any direct 22 way that -- that is clear to us. And that's the 23 point that I'm making. 24 Whether they happen to mention a few 25 risk factors for ovarian cancer in the tech --</p> | <p style="text-align: center;">Page 309</p> <p>1 question, it depends on the study. But I would 2 say generally that a meta-analysis should include 3 a qualitative review of the individual studies, 4 and that as part of that, if there are 5 epidemiologic studies, that would include a risk 6 of bias assessment, of which confounding is -- is 7 one risk of bias. 8 Q And if in a given meta-analysis the 9 authors don't include a qualitative review of the 10 individual studies, as a general proposition, that 11 would render their study potentially invalid or -- 12 MR. TISI: Objection. 13 BY MR. HEGARTY: 14 Q -- unreliable, correct? 15 MR. TISI: Objection. 16 THE WITNESS: I think again you're 17 asking me in the abstract, and I'm just going to 18 respond in the abstract that that is a general 19 process of a meta-analysis. I mean to what extent 20 any particular -- your interpretation of 21 qualitative, my interpretation of qualitative, a 22 particular author's description of what they did 23 or did not do, I would have to evaluate that on 24 a -- on a case-by-case basis. 25 But I -- I am willing to say, and I</p> |
| <p style="text-align: center;">Page 308</p> <p>1 excuse me, text of their paper, that doesn't meet 2 the bar. 3 Q At the very bottom of page 22, the 4 carryover sentence, you say: "They do not assess 5 the adequacy of control for confounding at the 6 individual study level." 7 Do you see where I'm reading? 8 A Yes. 9 Q So is it your testimony that if a 10 meta-analysis doesn't assess the adequacy of 11 control for confounding at the individual study 12 level for each of the studies in the 13 meta-analysis, the meta-analysis is invalid? 14 A Well, again, I'm going to -- I'm going 15 to caveat this with, you know, when you are 16 evaluating something, you are eval -- a study, a 17 meta-analysis, you are evaluating the totality of 18 it. 19 And in this case, I'm -- it's even taken 20 to another level because the authors continually 21 rely upon this position and advocate for this 22 particular position that uncontrolled confounding 23 may explain this positive association. 24 So to try to answer your question, I'm 25 going to say, you know, it depends on the research</p> | <p style="text-align: center;">Page 310</p> <p>1 agree, that a review of the individual studies is 2 part -- one of the first parts of a meta-analysis. 3 BY MR. HEGARTY: 4 Q Again, as a general proposition, would 5 you consider an error in a meta-analysis if the 6 authors did not do that? 7 MR. TISI: Objection. 8 MS. PARFITT: Objection. 9 THE WITNESS: I would consider it a 10 concern, yes. It would -- it would raise concern. 11 But, again, within -- I would have to see it -- 12 how that's being presented. How do I know that? 13 What are the methods? You know, how has 14 confounding been addressed? I think it's so 15 contextually specific that it's really hard to 16 answer that in the abstract. 17 BY MR. HEGARTY: 18 Q Over on -- at the top of page 23, you 19 say in the bolded part that: "The authors do not 20 provide any empirical evidence to support their 21 assertion that uncontrolled confounding may 22 explain the observed positive association between 23 talc exposure and ovarian cancer." 24 Do you see where I'm reading? 25 A I do.</p> |

April Zambelli-Weiner, Ph.D.

| Page 311 | Page 313 |
|---|---|
| <p>1 Q When you say "empirical evidence," what 2 do you mean? 3 A Oh, I'm sorry, I just coughed over your 4 question. 5 Q When you say "empirical evidence," what 6 do you mean? 7 A So empirical data, data from other 8 studies, data from their own sensitivity analyses, 9 demonstrating that, you know, there either is or 10 is not concern for a residual confounding. 11 Q So as a general proposition, is it your 12 testimony that if a meta-analysis fails to include 13 empirical data with regard to uncontrolled 14 confounding, the paper is invalid and unreliable? 15 MR. TISI: Objection. 16 THE WITNESS: No. I'm not going to 17 agree to that in the abstract. I think again you 18 can't take this analysis out of context, and the 19 fact that the authors repeatedly assert to the 20 FDA, to the medical and scientific community, that 21 uncontrolled confounding may explain this positive 22 association. I mean, it literally becomes a 23 mantra that almost takes on the feeling of -- of 24 fact, so this is repeatedly asserted. 25 And the point that I'm making is -- and</p> | <p>1 without providing data? 2 A Well, what I can say to you as -- as a 3 peer reviewer, as someone who's been on both sides 4 of the peer review process, it is -- it's 5 certainly not improper to hypothesize. Again, it 6 depends on how it's couched. 7 But what I will say is, as a general 8 rule, the conclusions must be supported with data. 9 So it's one thing to say something may cause 10 something or something may explain something or 11 this is a limitation that we weren't able to 12 explore fully. You know, it depends on how that's 13 being presented. 14 But I think that I can say, again having 15 been on both sides of that process, that if you're 16 going to come out strong on a position about 17 confounding, if you're going to say, This is 18 explained by uncontrolled confounding, or we are 19 confident that uncontrolled confounding is not a 20 strong risk of bias, you're going to be asked to 21 back that up with real data. 22 Q And what kind of real data would you 23 need to back that up? 24 A I think, as I said, data from other 25 studies, or the authors could do their own</p> |
| <p style="text-align: center;">Page 312</p> <p>1 we're still talking about the 2003 paper, as far 2 as from my understanding, is this mantra is 3 repeated throughout the paper without any actual 4 data to support that notion. 5 BY MR. HEGARTY: 6 Q So with regard to authors presenting 7 hypothesis, you would fault any author of a report 8 if they set forth a hypothesis that didn't -- that 9 wasn't supported by data, correct? 10 MR. TISI: Objection. 11 THE WITNESS: Not necessarily. It 12 depends how it's couched. It depends how it's 13 presented. Again, that's why I said you can't 14 really take this out of the context of -- of this 15 analysis of why this is so important. 16 And, you know, I can't recall their 17 specific comments off the top of my head. I'm 18 sure we could find them in their various -- 19 various papers, but they're very definitive, very 20 assertive about this as an explanation for the -- 21 the positive association that's observed. 22 BY MR. HEGARTY: 23 Q Can you cite for me any authority that 24 says it's improper for authors in an article like 25 this to hypothesize the reasons of the results</p> | <p style="text-align: center;">Page 314</p> <p>1 sensitivity analyses around -- around that 2 particular issue. 3 Q If you look at the next section at the 4 bottom of page 23, "Unsubstantiated Claims of 5 Selection Bias." Do you see that section? 6 A Yes. 7 Q You make reference there to Section 8 860.7. Correct? 9 A Yes, that's correct. 10 Q That section applies only to approval of 11 Class III medical devices, correct? 12 A Yes. That -- that is a section out of 13 the Medical Device Code, and I think I was simply 14 using that as an example of -- of guidance that's 15 out there for the scientific and regulatory 16 community. And I think that above that, I also 17 cite some other -- other examples for the point 18 I'm trying to make, which is the conclusions need 19 to be substantiated with data -- by the data or 20 with data. And I think that's the point I just 21 made -- 22 Q Well, can you cite -- 23 A -- previously. 24 Q I'm sorry. 25 Can you cite for me any text or</p> |

April Zambelli-Weiner, Ph.D.

| Page 315 | Page 317 |
|--|---|
| <p>1 authority by any author that says the section you 2 quoted there applies to epidemiologic studies like 3 the 2003 study by Huncharek?</p> <p>4 A Again, I don't know that -- that's kind 5 of a strange question to me, but I think I just 6 explained why I -- why I cited that there.</p> <p>7 Q Well, that section doesn't apply to 8 cosmetics, correct?</p> <p>9 A Well, again, it's a general principle, 10 which I've supported with other cites. So it was 11 just another example.</p> <p>12 Q Can you cite for me any epidemiologic 13 text or other authority that says anything similar 14 to this as related to epidemiologic studies?</p> <p>15 A It's entirely possible. I can't quote, 16 you know, textbooks as I sit here right -- right 17 at this moment.</p> <p>18 Q If you stay on page 24, at the very top, 19 you criticize the 2003 paper for proposing an 20 explanation for the spurious association between 21 talc use and ovarian cancer, saying that the 22 authors provided no substantive evidence or 23 discussion to support this supposition.</p> <p>24 Do you see where I'm reading?</p> <p>25 A I do. One second, please.</p> | <p>1 A I'm just -- I'm rereading your question. 2 I think this is the section -- let me 3 just look at it quickly.</p> <p>4 Right. Right. So this is -- this is I 5 think the section where I'm talking about the 6 imbalanced discussion around -- around this 7 particular issue.</p> <p>8 Q Well, are you aware of the possibility 9 of vaginal irritation and discharge post-ovarian 10 cancer surgery and treatment?</p> <p>11 A I would say generally, yes.</p> <p>12 Q And both of those conditions could 13 prompt talc use, correct?</p> <p>14 A Both of what conditions?</p> <p>15 Q Vaginal irritation and vaginal 16 discharge.</p> <p>17 A I'm sorry. What was your question 18 again?</p> <p>19 Q Both of those conditions, vaginal 20 irritation and vaginal discharge, could prompt 21 talc use, correct?</p> <p>22 MR. TISI: Objection.</p> <p>23 THE WITNESS: Sure. I mean, so could a 24 lot of other conditions as well.</p> <p>25 BY MR. HEGARTY:</p> |
| Page 316 | Page 318 |
| <p>1 One second.</p> <p>2 Q Do you see where I'm reading?</p> <p>3 A So you're at the top of page 24?</p> <p>4 Q Yes.</p> <p>5 A Yes.</p> <p>6 Q You later say that Huncharek went on to 7 admit in the 2009 response that there was no basis 8 for such an effect in the literature, correct?</p> <p>9 A Yes, I believe that's -- that's correct.</p> <p>10 Q So were they correct -- was Huncharek 11 correct in the 2009 response to FDA?</p> <p>12 A I -- I didn't evaluate the -- you know, 13 his -- his statement later. So I think the point 14 that I'm making is -- again, we're in the 2003 15 paper, so within that context, they're offering up 16 this bias as an explanation for the positive 17 association, and within the context of that paper, 18 they don't provide any data to really support 19 that.</p> <p>20 Q In the paragraph beginning "The authors 21 also single out" -- do you see that paragraph?</p> <p>22 A Yes.</p> <p>23 Q You refer to the authors omitting 24 discussion about the treatment effect in the 25 hospital-based case-control studies, correct?</p> | <p>1 Q Well, you're aware that Dr. Huncharek is 2 a radiation oncologist, correct?</p> <p>3 A I think you -- I think you mentioned 4 that before. I'm not aware of his -- you know, 5 his specific background.</p> <p>6 Q So is there anything wrong with someone 7 with direct personal knowledge of a condition 8 post-treatment with making references to that 9 knowledge in an article like this?</p> <p>10 A I don't think that's the issue that I'm 11 making at all. I think the issue that I'm making 12 is, you know, they raise this as a -- as a 13 possibility. Nothing wrong with raising that as a 14 possibility as a hypothesis. The point is they 15 don't substantiate it with any data.</p> <p>16 They further then don't go on to discuss 17 the flip side of this issue, which is that the 18 hospital-based case-control studies, which, by the 19 way, are historically known to be at higher risk 20 of bias than population-based case-control 21 studies, may also be at risk of treatment bias 22 because of the nature of the controls in those 23 studies.</p> <p>24 And when we're talking about 25 misrepresentations, you know, in the studies, in</p> |

April Zambelli-Weiner, Ph.D.

| Page 319 | Page 321 |
|---|---|
| <p>1 the two -- in the 2003 paper, the authors, if I'm 2 recalling correctly, make an assertion that the 3 rate of exposure in the control groups is actually 4 comparable between the population and 5 hospital-based case-control studies. And my 6 inspection of those -- of some of those studies is 7 that that is not in fact true. So in fact, there 8 is a possibility that the hospital-based 9 case-control studies may be at higher risk of bias 10 due to this issue than the population-based 11 case-control studies.</p> <p>12 So what I'm detailing in this paragraph 13 is their imbalanced discussion of this issue, 14 which really drives at the results and the 15 interpretation of the population- versus 16 hospital-based case-control studies.</p> <p>17 Q Well, you say in this paragraph that the 18 controls with gastrointestinal cancers and skin 19 cancer, as well as other diseases -- you cite 20 hemorrhoids, urinary disease, skin disease -- 21 could prompt short-term talc use.</p> <p>22 You cite no substantiation for those 23 statements, do you?</p> <p>24 A Correct. Here, I believe that's 25 correct. But, again, I'm not proffering this out</p> | <p>1 publication, then their analysis is invalid and 2 unreliable?</p> <p>3 MR. TISI: Objection. 4 THE WITNESS: No, that's -- that's not 5 what I'm saying. I wouldn't characterize it that 6 way.</p> <p>7 I think, you know, what I'm saying again 8 is that if you are going to put forward this -- 9 this concept or this idea that this type of bias 10 is at play and can explain the observed positive 11 associations, that that requires support and that 12 requires a fulsome discussion. I mean, it's well 13 known in the field of epidemiology that 14 hospital-based case-control studies are at a 15 higher risk of bias.</p> <p>16 And by the way, going back to my 17 previous question whether that can be 18 substantiated or not, what I wrote there, the data 19 are the data, and the data in some of the studies 20 actually show that the control groups do have a 21 higher prevalence of talc exposure, the 22 hospital-based case-control studies, than some of 23 the population-based case-control studies. So the 24 data actually bear out regardless of whether that 25 particular statement can be substantiated.</p> |
| Page 320 | Page 322 |
| <p>1 as an example of this -- this explains the 2 positive association. I'm not putting this 3 forward to the FDA and to the medical and 4 scientific community and saying, You know, this is 5 proof that this positive association is noncausal.</p> <p>6 I'm simply raising here the issue, the 7 methodologic issue that the authors have failed to 8 have an imbalance -- or a balanced, excuse me, 9 discussion of this particular issue.</p> <p>10 Q Well, can you substantiate in any way by 11 citing to any authority that any of the conditions 12 you cite would prompt talc use?</p> <p>13 A I -- I don't know. It might -- might be 14 possible.</p> <p>15 Q You say in the last paragraph before the 16 Conclusion section that -- again, the section 17 we're talking about that you're -- and you just 18 mentioned it before, that the authors failed to 19 present a balance -- or I think you said the 20 authors present an imbalanced discussion of the 21 potential impact with regard to hospital- versus 22 population-based studies, correct?</p> <p>23 A Correct.</p> <p>24 Q And what you're saying is that if an 25 author doesn't give equal time to both sides in a</p> | <p>1 BY MR. HEGARTY: 2 Q Cite for me any -- cite for me the 3 authority that says that hospital-based 4 case-control studies are at higher risk of bias. 5 A Epi -- any epi textbook. 6 Q Cite for me an epi textbook. 7 A Rothman. 8 Q Okay. You said a moment ago that if you 9 are going to put forward this concept or this idea 10 that this type of bias is at play, it can explain 11 the observed positive associations that that 12 requires support. 13 The same would be true in any 14 publications or report where you're putting forth 15 any kind of concept, whether it's bias or anything 16 else from the epidemiologic studies, you have to 17 in that situation require support for what you're 18 saying, correct? 19 MR. TISI: Objection. 20 THE WITNESS: Again, I'm going to go 21 back to what I -- what I said previously and try 22 to repeat it accurately. It really depends on the 23 context of which -- of what you're saying and how 24 you're saying it. 25 So, I mean, certainly in a peer-reviewed</p> |

April Zambelli-Weiner, Ph.D.

| Page 323 | Page 325 |
|---|---|
| <p>1 publication, as I said before, it's kind of prime 2 real estate. You can't address every possible 3 thing under the sun. And so it depends on how 4 it's being proffered. It's one thing to say, You 5 know what, this is a limitation of our study. We 6 were unable to address this, or, you know, this is 7 a strength of our study. Certainly those kinds of 8 qualitative discussions exist, and you can't 9 possibly provide data to support all of those. 10 But this is a very different situation. 11 These are two concepts that are being repeatedly 12 offered up over the period of a decade to a 13 regulatory agency, to the medical and scientific 14 community, as the reason -- some of the prime 15 reasons why this is not a causal association. 16 That's a very different situation. 17 BY MR. HEGARTY: 18 Q What -- strike that. 19 Is it your contention that -- strike 20 that. 21 Is it improper in any analysis, whether 22 it's published or in a report, to include an 23 imbalanced discussion of a particular issue? 24 MR. TISI: Objection. Beyond the scope. 25 THE WITNESS: Can you repeat that,</p> | <p>1 (Exhibit No. 18 was marked for 2 identification.) 3 BY MR. HEGARTY: 4 Q If you turn over to page 26 in your 5 report, Table 3, please. 6 A Yes. 7 MR. TISI: You're -- the copy you're 8 marking has handwritten notes on it. Is this -- 9 MR. HEGARTY: Let me see it. Did I give 10 you one that -- it might have been one of mine. 11 Oh, it's on the -- I'll take it back. 12 MR. TISI: It's on this one too. 13 MR. HEGARTY: Oh, it's handwritten 14 notes? 15 MR. TISI: It just says -- I mean, I 16 haven't gone through the paper, but right here 17 where the -- 18 MR. HEGARTY: Oh, okay. Fine. 19 MR. TISI: No, I just don't know if that 20 was intentional or not. 21 BY MR. HEGARTY: 22 Q So we're focusing on your Table III on 23 page 26. 24 A Okay. 25 Q You claim that the -- strike that.</p> |
| <p>1 please? 2 BY MR. HEGARTY: 3 Q Sure. Is it improper in any analysis, 4 whether it's published or in a report, to include 5 an imbalanced discussion of a particular issue, 6 only focusing on literature going a certain way 7 and not talking about literature going the other 8 way? 9 MR. TISI: Objection. 10 THE WITNESS: Well, I -- again, that's a 11 very broad question. So I think it would depend 12 upon the nature of -- of the report, of the paper, 13 of the question, of the particular issue. You 14 just can't kind of answer that in a vacuum. 15 That -- that's very difficult. 16 BY MR. HEGARTY: 17 Q If you turn over to Section 6.2 of your 18 report, this section starts discussing the 2007 19 diaphragm paper, correct? 20 A Correct. 21 Q Do you have a copy of that in front of 22 you? 23 A Yes, I do. 24 Q And for purposes of the record, I'm 25 going to mark that paper as Exhibit 18.</p> | <p>1 How did the misreference to Richardson 2 affect the substantive results of this paper? 3 A I'm just rereviewing for a moment. 4 (Peruses document.) 5 I think this is the -- you know, again, 6 the same answer for -- for this table as it was 7 for Table I in my report. Which would be, you 8 know, anything that drives at the -- you know, a 9 clear articulation of the methods and a clear 10 understanding of what was done and the results, to 11 me is a substantive error. Again, with the caveat 12 that these all exist on a backdrop of -- of other 13 errors. You know, you can't really take a single 14 error in isolation. It's -- it's a review of the 15 totality of the paper. 16 Q Your next point in the table refers to 17 the difference between the text -- what the text 18 is reporting and what the table shows, correct? 19 A Right. Correct. So -- I just want to 20 pull up the paper -- or the table real fast just 21 to make -- make the comment clear. 22 So this is a little bit of a compound 23 issue. So, I mean, in the text they cite an odds 24 ratio of 0.6 for Booth. The first issue is that 25 0.6 is associated with a different study, Ness.</p> |

April Zambelli-Weiner, Ph.D.

| Page 327 | Page 329 |
|--|---|
| <p>1 But the second issue, which may be in 2 another row, but I -- I don't recall, is that then 3 in Table I, the adjusted odds ratio for Booth that 4 is reported, which is 0.75, actually does not 5 exist in Booth. So that --</p> <p>6 Q Well -- okay. Are you finished?</p> <p>7 A Sure.</p> <p>8 Q Well, your -- you say in your report 9 that in Table I, the lowest adjusted OR is 0.6, 10 correct? That's what you say in your report.</p> <p>11 A Correct. Right.</p> <p>12 Q That's not right, is it? The lowest 13 adjusted risk is from Harlow and Weiss, and that's 14 0.5, correct?</p> <p>15 A That's correct. So I guess -- I guess I 16 was referencing their statement, but their 17 statement is also incorrect in that aspect as 18 well. So, yes.</p> <p>19 Q Well, actually, in your report, you're 20 saying -- you drew out the number and said the 21 lowest number was 0.6, didn't you?</p> <p>22 A Again, referencing their range, so, you 23 know, in theory, they're both -- they're both 24 incorrect, yes.</p> <p>25 Q But your report is not correct, right?</p> | <p>1 definition of -- of a "substantive error."</p> <p>2 Q The next reference includes reporting -- 3 or strike that.</p> <p>4 The next reference refers to the 5 inclusion of Booth in the paper. Do you see where 6 I'm reading?</p> <p>7 A Are you in the third one down?</p> <p>8 Q The third one down.</p> <p>9 A Yes.</p> <p>10 Q Is it your -- your statement in your 11 report is that Booth should have never been 12 included in the analysis, correct?</p> <p>13 MR. TISI: Objection.</p> <p>14 THE WITNESS: I think that's one of the 15 comments that I'm making, and I think that we 16 could talk about that, because that's obviously 17 something that the authors bring up as well and 18 do -- do an analysis dropping -- dropping Booth.</p> <p>19 But I think the other point which is 20 perhaps, you know, equally important is that this 21 particular adjusted odds ratio is not, you know, 22 what is in the original study. This is not 23 reported in the original study.</p> <p>24 BY MR. HEGARTY:</p> <p>25 Q Did you do the analysis excluding Booth?</p> |
| <p>1 MR. TISI: Objection.</p> <p>2 THE WITNESS: I think I just answered 3 that.</p> <p>4 BY MR. HEGARTY:</p> <p>5 Q Well, is the -- is the lowest adjusted 6 OR, as you report in your report, 0.6?</p> <p>7 MR. TISI: Objection.</p> <p>8 THE WITNESS: No, I agree with you that 9 the lowest adjusted OR is 0.5, and just explained 10 that, you know, I was referencing their comment on 11 the range of -- of odds ratios, which is also 12 incorrect.</p> <p>13 BY MR. HEGARTY:</p> <p>14 Q If you turn over to the next page, 15 page 27, the second cell down, how is the -- the 16 reversing of the descriptions of the Hartge and 17 Ness studies a substantive error in this paper?</p> <p>18 A Again, I'm sort of standing by my -- my 19 statements I've been giving you all morning, which 20 is, you know, an accurate description of the 21 methods is -- is paramount to a meta-analysis. 22 And I think for someone who's, you know, not 23 familiar with the literature, someone may apprise 24 these types of studies differently. And I -- it 25 is a substantive error as it relates to my</p> | <p>1 A No, I don't believe I did.</p> <p>2 Q Well, what would have been the effect of 3 the results if Booth had not been included?</p> <p>4 A Again, you know, same answer as -- as 5 we've been doing all morning. I didn't do that, 6 it wasn't my charge, and really we shouldn't be in 7 a position to have to -- to wonder and ask that 8 question.</p> <p>9 Q Well, you're the one, Doctor, who 10 claim -- has been claiming that this had an 11 improper -- or that this influenced regulators and 12 other authorities in an improper way.</p> <p>13 What would the numbers have been if they 14 had done the proper way?</p> <p>15 A It's -- it's not my job. I mean, that's 16 not -- that's a whole project unto itself. I 17 mean, you would have to strip it back and go all 18 the way back to the beginning, and that just 19 wasn't what I was tasked with doing. I mean, I 20 think the issue is -- is exactly what these papers 21 are and how they were -- how they were put 22 forward, as you just said.</p> <p>23 Q The next reference again to Harlow and 24 Weiss, did you run the analysis excluding Harlow 25 and Weiss?</p> |

April Zambelli-Weiner, Ph.D.

| Page 331 | Page 333 |
|---|---|
| <p>1 MR. TISI: Well, the next reference is 2 Harlow and the next -- 3 MR. HEGARTY: Im sorry. 4 MR. TISI: Are you skipping two cells 5 down? 6 MR. HEGARTY: Yeah. Let me go back. 7 BY MR. HEGARTY: 8 Q The next reference is to Harlow. Did 9 you run the analysis without including Harlow? 10 A The same answer. 11 Q No? 12 A No, for the reasons I just -- I just 13 described. 14 Q Well, what effect did it have on the 15 numbers reported in the study by including Harlow? 16 A Same answer. Same answer as before. 17 Q Which is? 18 A Which is, again, not my charge, didn't 19 do it, and same answer as before. 20 Q The next point as to Harlow and Weiss, 21 did you run the analysis without including Harlow 22 and Weiss? 23 A No. Same answer as before. 24 Q What would have been the effect on the 25 numbers reported or the conclusions drawn if</p> | <p>1 to that. 2 BY MR. HEGARTY: 3 Q Well, your odds ratios are actually 4 lower than the 2007 article reported, correct? 5 A Again, the point -- the point of this 6 table, I'm not endorsing this analysis. I'm not 7 endorsing this study. So I wouldn't interpret it 8 that way. The only conclusion that I would draw 9 from this table is that their main pooled analysis 10 cannot be replicated. 11 Q Going back to my question, though, your 12 odds ratios were actually lower than what the 2007 13 article reported, correct? 14 A That's correct. 15 Q And your odds ratios support the 16 conclusions reached in the 2007 article, correct? 17 MR. TISI: Objection. Misstates. 18 THE WITNESS: No, I -- I wouldn't -- I 19 wouldn't agree with that. Again, I -- I'm not 20 endorsing this analysis. I think there's a lot of 21 issues with this paper. You're sort of picking 22 out one, and I -- I wouldn't agree to that, no. 23 BY MR. HEGARTY: 24 Q Well, an odds ratio of 0.74 would 25 suggest no association between talc-dusted</p> |
| Page 332 | Page 334 |
| <p>1 Harlow and Weiss had not been included? 2 A I can't answer that because I didn't do 3 that. 4 Q Over on page 29, Table IV, you report on 5 your attempted -- attempt at replication of the 6 numbers from the 2007 paper, correct? 7 A Correct. 8 Q In all your efforts, all the analyses 9 you did, you calculated an odds ratio each time 10 less than 1, correct? 11 A That is correct. 12 Q Using the fixed effect model, you showed 13 a statistically significant odds ratio of 0.74, 14 which would be a protective effect against ovarian 15 cancer, correct? 16 MR. TISI: Objection. 17 THE WITNESS: Well, you're -- so I'm 18 going to answer that to the best of my ability, by 19 saying we haven't established the validity of this 20 analysis at face value. So I'm not agreeing with 21 that finding that I would draw that conclusion 22 from it. 23 But I can simply tell you that based on 24 my attempted replication of their analysis, that 25 is the result. So I can -- I can definitely agree</p> | <p>1 diaphragms and ovarian cancer, correct? 2 A Well, in a vacuum, if you're just -- if 3 you're just taking an odds ratio and a confidence 4 interval and saying how do you interpret this, 5 that is true. But I think it's important to 6 remember that there are errors in this data, and 7 in fact, you know, if I'm recalling correctly, one 8 really important error where, you know, the 9 confidence interval and the point estimate didn't 10 even make sense. So you're -- you're -- this is 11 based on a flat analysis. This was just an 12 attempt to replicate. 13 Q Did you review the Penninkilampi study? 14 A I -- I don't recall if I reviewed that 15 study at some point. 16 MR. HEGARTY: I'm going to mark as 17 Exhibit 19 the Penninkilampi study. 18 (Exhibit No. 19 was marked for 19 identification.) 20 MR. TISI: Just object. Outside -- 21 THE WITNESS: Would this -- 22 MR. TISI: Object. Outside the scope. 23 THE WITNESS: Would this be another good 24 time to -- if we're taking a shift, just to take a 25 quick bathroom break?</p> |

April Zambelli-Weiner, Ph.D.

| Page 335 | Page 337 |
|--|---|
| <p>1 MR. HEGARTY: Sure. 2 THE WITNESS: Okay. Thanks. 3 MR. HEGARTY: Go off the record. 4 THE VIDEOGRAPHER: The time is 12:16 5 p.m. We're going off the record. 6 (Lunch recess.) 7 THE VIDEOGRAPHER: The time is 1:07 p.m. 8 and we're back on the record. 9 BY MR. HEGARTY: 10 Q Doctor, when I left off, we were going 11 to look at the Penninkilampi study, but before I 12 get there, I wanted to take a step back real 13 quick. 14 With regard to the 2003 and 2007 studies 15 you talk about in your report, those studies are 16 meta-analyses of case-control studies, correct? 17 A I don't believe they're limited to 18 case-control studies. I -- 19 Q Well, the -- 20 A I'd have to go back and look. 21 Q Well, the 2007 diaphragm study looked at 22 case-control studies, correct? 23 A Could we look at it? 24 Q Well, what other kind of study could 25 they look at?</p> | <p>1 A That's correct, yes. 2 Q And you presented this with -- 3 A This was a presentation to -- 4 Q -- John Clark? 5 A -- to defense firms with a panel. Yes, 6 correct. 7 Q You presented this with John Clark, 8 correct? 9 A He was one of the presenters, yes. 10 Q And over on several pages into it, if 11 you find the page that says "Strengths and 12 Limitations of Observational Studies." 13 A I'm sorry. Where are you? 14 Q Let me see your copy. 15 Do you see where I'm pointing now that 16 says, "Strengths and Limitations of Observational 17 Studies"?: 18 A Yes. 19 MR. TISI: I'm sorry, what page number 20 are you on here? 21 MR. HEGARTY: There's not a page number. BY MR. HEGARTY: 23 Q One of the limitations is, is subject to 24 many biases. Do you agree with that statement? 25 A I would say generally again that</p> |
| <p>1 A Cohort study. 2 Q Okay. Well, they -- they didn't -- you 3 do agree they did look at case-control studies, 4 correct? 5 A Correct. 6 Q And case-control studies are subject to 7 many biases, correct? 8 A I don't think I'd agree with your 9 characterization of that just in the abstract. I 10 think I would agree that all study designs have 11 strengths and limitations. 12 MR. HEGARTY: I'll mark this as Exhibit 13 20. 14 (Exhibit No. 20 was marked for 15 identification.) 16 MR. HEGARTY: I'm sorry. You need the 17 copy. 18 MR. TISI: Thanks. BY MR. HEGARTY: 20 Q This is a copy of a PowerPoint that you 21 prepared; isn't that correct, Doctor? 22 A I participated in this. I don't recall 23 who prepared the PowerPoint. 24 Q Well, if you look over several pages in, 25 you see your picture, correct?</p> | <p>1 observational studies juxtaposed to RCTs are at 2 risk of bias, and that's what an analysis of 3 internal validity is. 4 Q But did you prepare this slide? 5 A I don't recall who prepared the slide. 6 Q You prepared -- you were part of this 7 presentation, though, correct? 8 A I was, correct. 9 Q And you participated in the preparation 10 of this slide deck, correct? 11 A I don't recall. 12 Q So is it your testimony that you can't 13 say that observational studies are subject to many 14 biases? 15 A I think I just answered your question 16 about that. 17 Q It's a true statement, though, correct? 18 A I think I just answered it. 19 Q What is the answer? 20 A I think I said observational studies 21 juxtaposed to RCTs are at risk of bias. 22 Q You don't make that limitation, though, 23 in this slide, do you? 24 A I don't remember -- 25 Q There's no reference to RTC studies, is</p> |

April Zambelli-Weiner, Ph.D.

| Page 339 | Page 341 |
|--|--|
| <p>1 there?</p> <p>2 MR. TISI: You're going to have to let</p> <p>3 her finish, Mark.</p> <p>4 MR. HEGARTY: I wasn't finished with my</p> <p>5 question.</p> <p>6 MR. TISI: Okay. Well, then --</p> <p>7 THE WITNESS: My apologies. Go ahead.</p> <p>8 MR. TISI: -- go ahead.</p> <p>9 BY MR. HEGARTY:</p> <p>10 Q There is no reference to RCT studies in</p> <p>11 this slide, correct?</p> <p>12 A Again, I'm just going to say I haven't</p> <p>13 seen this in a long time. I don't remember the</p> <p>14 context of these slides. On this particular</p> <p>15 slide, you're correct, there's no -- there's no</p> <p>16 mention of RCTs.</p> <p>17 Q Case-control studies or observational</p> <p>18 studies, correct?</p> <p>19 A They are one type of observational</p> <p>20 study.</p> <p>21 Q And you also say: "Observational</p> <p>22 studies are -- have limited control over</p> <p>23 composition of the control groups."</p> <p>24 That's correct, isn't it?</p> <p>25 A I would say, again, having not looked at</p> | <p>1 point?</p> <p>2 A Again, I think without -- without</p> <p>3 refreshing on this, I'm going to agree that you</p> <p>4 read that correctly, and I'm going to agree that</p> <p>5 it appears that what we're doing is juxtaposing</p> <p>6 clinical trials with observational studies. But I</p> <p>7 haven't looked at this in a very long time.</p> <p>8 Q And observational studies, as you say,</p> <p>9 data more likely -- is more likely to be</p> <p>10 incomplete and poorer quality, correct?</p> <p>11 A That's -- that's what's on the slide.</p> <p>12 Q That's a true statement, though,</p> <p>13 correct?</p> <p>14 A I would say again generally, not looking</p> <p>15 at the whole context of this, juxtaposed to RCTs,</p> <p>16 that is -- that is probably an accurate statement.</p> <p>17 Q If you'd turn to the Penninkilampi study</p> <p>18 that we had marked as Exhibit 19.</p> <p>19 First of all, have you ever read this</p> <p>20 study?</p> <p>21 A I don't recall.</p> <p>22 Q Are you able to say one way or the</p> <p>23 other?</p> <p>24 A No.</p> <p>25 Q If you look over on page -- on page 44</p> |
| <p style="text-align: center;">Page 340</p> <p>1 this in a long time -- well, actually, now looking</p> <p>2 up above two slides and seeing clinical trials, I</p> <p>3 can say for certain that this is really being</p> <p>4 juxtaposed to RCTs, so discussing the differences</p> <p>5 between RCTs and observational studies.</p> <p>6 Q Doctor, is it a true statement that</p> <p>7 observational studies have limited control over</p> <p>8 composition of the control groups?</p> <p>9 A I would say that I would agree with that</p> <p>10 as a limitation juxtaposed to RCTs.</p> <p>11 Q Is it true that observational studies</p> <p>12 have a limitation of standardization of exposures</p> <p>13 and outcome varies?</p> <p>14 Let me restate it that the -- for</p> <p>15 observational studies, standardization of exposure</p> <p>16 and outcomes vary, correct?</p> <p>17 MR. TISI: Let me place an objection.</p> <p>18 And if you need to kind of refresh</p> <p>19 yourself, you haven't seen this for a while, to</p> <p>20 realize the context, feel free to look at the</p> <p>21 document.</p> <p>22 THE WITNESS: Sure. I'm sorry, can you</p> <p>23 repeat --</p> <p>24 BY MR. HEGARTY:</p> <p>25 Q Do you agree with that third bullet</p> | <p style="text-align: center;">Page 342</p> <p>1 of this study.</p> <p>2 MR. TISI: Well, if you need to review</p> <p>3 it, and this is -- you've never read it before or</p> <p>4 you have -- feel free to do it. I'm going to</p> <p>5 object to any questions about Penninkilampi as</p> <p>6 being beyond the scope.</p> <p>7 THE WITNESS: (Perusing document.)</p> <p>8 BY MR. HEGARTY:</p> <p>9 Q Do you see in Table 1 --</p> <p>10 MR. TISI: Well, no. She's reading it.</p> <p>11 She's looking at it.</p> <p>12 MR. HEGARTY: Well, I haven't asked a</p> <p>13 question. I just --</p> <p>14 MR. TISI: Well, but you're about to ask</p> <p>15 a question about the study --</p> <p>16 MR. HEGARTY: Then we're going to go off</p> <p>17 the record.</p> <p>18 MR. TISI: No, we're not going to go off</p> <p>19 the record. It's not within the scope of her</p> <p>20 report. It's not cited, nothing. So if you're</p> <p>21 going to ask her questions about something --</p> <p>22 questions that are outside the scope of her</p> <p>23 report, and you give her a study and she's never</p> <p>24 read it before, she's going to read it.</p> <p>25 MR. HEGARTY: Well, we're not going to</p> |

April Zambelli-Weiner, Ph.D.

| Page 343 | Page 345 |
|--|--|
| <p>1 sit here while she reads it. 2 MR. TISI: Well, then, don't ask her -- 3 MR. HEGARTY: Let's go off the record. 4 MR. TISI: No, we're not going to go off 5 the record. We will not go off the record, and 6 we'll call the judge -- Judge Walsh if you want 7 to. 8 MR. HEGARTY: Okay. Well, let's call 9 him. 10 MR. TISI: Let's go. 11 MR. HEGARTY: Off the record. 12 MR. LOCKE: Yeah, let's go off the 13 record while we get that set up. 14 THE VIDEOGRAPHER: The time is 1:13 p.m. 15 We're going off the record. 16 (A discussion was held off the record.) 17 THE VIDEOGRAPHER: The time is 18 1:22 p.m., and we're back on the record. 19 BY MR. HEGARTY: 20 Q Doctor, we -- we were going to talk 21 about Penninkilampi. I'm going to table that 22 exhibit for right now, and I'm going to move on to 23 another part of your report. 24 If you would turn to page 36 of your 25 report, the section "PCPC 2009 Response." Do you</p> | <p>1 (Exhibit No. 22 was marked for 2 identification.) 3 BY MR. HEGARTY: 4 Q Is that the Chang study that's 5 referenced in your table? 6 A Yes, I believe so. Let me just check. 7 (Peruses document.) 8 Yes. 9 Q If you look over on Table 2 of the Chang 10 study, Exhibit 22, that is the dose-response data 11 reported in the study, correct? 12 A Can I just have a minute to look at 13 this? (Peruses document.) 14 So I would say there is dose-response 15 data reported in Table 2 of the Chang study, but 16 I'm not certain that's the only dose-response data 17 that's in the paper. 18 Q Well, I -- I'm focusing on the dose- 19 response data in Table number 2. 20 A Okay. 21 Q The data for after-bath use shows 22 decreasing odds ratios as dose increases, correct? 23 A I'm sorry, after bath talc use, is that 24 what you said? 25 Q Yes.</p> |
| <p>1 see that section? 2 A Yes, I do. 3 Q This is your analysis of the 2009 4 response to the Citizen Petition, correct? 5 A Yes, that's correct. 6 Q I'm going to mark as Exhibit 21 a copy 7 of that response. 8 MR. TISI: Thank you. 9 (Exhibit No. 21 was marked for 10 identification.) 11 BY MR. HEGARTY: 12 Q Do you see the -- see what I marked as 13 Exhibit 21? 14 A Yes. 15 Q And is that the document you reviewed 16 for purposes of this part of your report? 17 A Yes, I believe so. 18 Q Over on page 37 of your report, in the 19 table included there, Table VI, you make reference 20 to statements that the authors of the response 21 made about the Chang 1997 study, correct? 22 A Correct. 23 MR. HEGARTY: I'm going to mark as 24 Exhibit 22 the Chang study that is referenced in 25 your table.</p> | <p>1 A That -- that's correct, yes. 2 Q The authors then say in the response as 3 you note that that data suggests an inverse 4 dose-response. 5 How is that statement wrong based on the 6 data from Table 2 in the Chang study? 7 A Well, again, you know, I think this is 8 a -- a broader issue of the discussion of 9 dose-response. As I indicated, this is not the 10 only dose-response data in -- in the Chang study. 11 And I think that this really drives at the lack of 12 a fulsome discussion of the reasons why one might 13 not observe a dose-response. I think that's an 14 incomplete representation of the authors' study 15 and the authors' data, and really drives at one of 16 the very important issues in dose-response 17 analyses, which is taking a quantitative variable 18 and reducing it into arbitrary categories. 19 And so a very important piece of data 20 from the Chang study was ignored, which is the 21 fact that when they looked at these variables 22 quantitatively, they did see a dose-response 23 increasing risk with increasing years of -- now 24 that's years of talc exposure. So just to be -- 25 just to be accurate, I want to be sure that I'm</p> |

April Zambelli-Weiner, Ph.D.

| Page 347 | Page 349 |
|--|---|
| <p>1 being accurate with -- with what I have in my 2 report. 3 Q So how is it wrong to say as the 4 response does that the data suggests an inverse 5 dose-response? What's inaccurate about that 6 statement? 7 A It's misleading. It's a mis-- it's a 8 -- misleading and non-wholistic, and in my -- and 9 in my opinion, not a responsible, fulsome 10 discussion of dose-response, both of dose-response 11 at large. 12 And if you're going to advocate in the 13 way that these authors and PCPC advocated for lack 14 of dose-response as a key reason there's not a 15 causal relationship, then I feel there's a 16 scientific obligation to provide a fulsome 17 discussion of that, which the authors do not do. 18 They ignore the data that does not line up with 19 their -- with their opinion, and they don't talk 20 about the reasons why one might not observe a 21 dose-response, and the reasons why one might 22 observe an inverse dose-response. Because there 23 are actually scientifically defensible reasons why 24 you might observe an inverse dose-response in a 25 causal relationship.</p> | <p>1 risk of ovarian carcinoma. Questionable trends in 2 duration and frequency of exposure suggest that 3 further studies may be needed to clarify the role 4 of talc and the etiology of this disease." 5 So how is it wrong to say they 6 acknowledge that a lack of a dose-response needs 7 clarification? 8 A I think I just explained my -- my issue 9 with their treatment of this paper. 10 Q But how is it wrong? 11 A What's wrong is the incomplete and 12 unacknowledged -- the title of the -- of the table 13 is "Unacknowledged Positive Dose-Response Data." 14 That's the title of the table. So that's the 15 point that I'm illustrating and calling out here 16 is that they did not address the positive 17 dose-response data that was observed in the study. 18 Q Was it your testimony that scientists 19 are not allowed in studies to look at other papers 20 and state any disagreements that they have with 21 the authors? 22 A Can you repeat that, please? 23 Q Is it your testimony that in reviewing 24 another author's paper that it's improper to draw 25 your own conclusions and report those own</p> |
| <p>1 Q Did you do that analysis for the Chang 2 study? 3 A I was not charged with doing that 4 analysis. So, again, I am critically reviewing 5 the Huncharek and Muscat papers, you know, as they 6 were presented and evolved over time, and 7 advocated to FDA and to the medical and scientific 8 community. 9 Q They say in that -- you say in that 10 table that Huncharek and Muscat say they 11 acknowledge that the lack of dose-response needs 12 clarification. 13 That's a true statement from the Chang 14 study, correct? 15 A Well, I -- I'd have to read -- 16 Q Well, look at the conclusion in the very 17 first -- on the very first page of the Chang 18 study. And I'll read it for purposes of the 19 record. 20 The conclusion says -- 21 A Can you tell me where you are? I'm 22 sorry, excuse me. 23 Q The very first page. The conclusion 24 says: "This investigation supports previous 25 contentions that exposure to talc may increase</p> | <p>1 conclusions in your paper? 2 A I'm certainly not saying that it's wrong 3 for people to disagree, but I -- as -- as someone 4 who is in the business of designing and 5 implementing studies that get submitted to FDA, I 6 can say that that warrants a fulsome and complete 7 and accurate discussion of the issue if you are 8 going to put forward this lack of dose-response as 9 a primary reason why you believe there's not a 10 causal association. I feel very strongly about 11 that. 12 Q And if somebody takes the opposite view 13 that there is a dose-response, you would also take 14 issue if they failed to support that contention 15 with a fulsome and complete and accurate 16 discussion, correct? 17 MR. TISI: Objection. 18 THE WITNESS: Again, you're taking -- 19 you're sort of taking my statement a little bit 20 out of context, because what happens in a 21 particular manuscript depends on the context, what 22 happens in a particular manuscript or whatever the 23 forum is for that discussion. 24 The point here is, and I think we're in 25 the section -- yeah, we are -- we're in the</p> |

April Zambelli-Weiner, Ph.D.

| Page 351 | Page 353 |
|---|--|
| <p>1 section on the PCPC report -- this was not a 2 manuscript that was restricted in word count. 3 This is a report in which they had the opportunity 4 to provide as much detail, as much of a fulsome 5 discussion as was necessary to shed light on 6 these very important issues, and they did not do 7 that.</p> <p>8 BY MR. HEGARTY:</p> <p>9 Q So in any report where you're not 10 limited by space or word count, if you fail to 11 provide that fulsome discussion in order to 12 support a proposition that you're making, then you 13 would take issue with that, correct?</p> <p>14 MR. TISI: Objection.</p> <p>15 THE WITNESS: Again, I'm going to 16 disagree with your blanket characterization, and 17 say, you know, I can comment on this particular -- 18 these particular studies, this particular context, 19 and the submission of this data and the posturing 20 of the data to the FDA. That's what I'm 21 commenting on.</p> <p>22 There's all kinds of contexts and 23 reasons and reports that get written for various 24 purposes. So that's just an overly broad question 25 that I really can't answer. I -- I provided you</p> | <p>1 A I do. 2 Q Okay. 3 A Would you like to point me to a 4 particular area? 5 Q Then if you turn over to page -- first 6 of all, Harlow wasn't included in those 12 studies 7 that the Citizen Petition included in its 8 submission to FDA, was it? 9 A I -- I don't recall specifically. 10 Q Well, you had -- do you have the exhibit 11 for the Citizen Petition in front of you? 12 A Let me find it. 13 Q That's Exhibit 13. 14 A Yes. 15 Q Is Harlow listed as one of the 16 authorities? 17 A Does not appear to be, no. 18 Q So it would not be proper to include a 19 discussion about Harlow in the first part where 20 they say they're only going to address the 12 21 studies cited in the Citizen Petition, correct? 22 MR. TISI: Objection. 23 THE WITNESS: I don't necessarily agree 24 with that, no. 25 BY MR. HEGARTY:</p> |
| <p>1 with my opinion and basis for this table. 2 BY MR. HEGARTY:</p> <p>3 Q The next comment you make in that table 4 is as to Harlow 1992, correct?</p> <p>5 A Yes.</p> <p>6 Q And you say that Huncharek and Muscat 7 provided no discussion of Harlow 1992, correct?</p> <p>8 A As far as I can recall, that's -- that's 9 correct.</p> <p>10 Q Did you read their response?</p> <p>11 A I'm sorry?</p> <p>12 Q The two thousand -- did you read the 13 2009 response?</p> <p>14 A Yes, I did.</p> <p>15 Q Did you see that in the first part of 16 the 2009 response, that they addressed each of the 17 12 references that were included in the PCPC 18 response? Do you understand that?</p> <p>19 I'm sorry, that were in the --</p> <p>20 A Would you like to point to where --</p> <p>21 Q -- that were in the Citizen Petition.</p> <p>22 Do you understand that the first part of 23 the response was to address the 12 studies that 24 were included in the Citizen Petition? Do you 25 understand that?</p> | <p>1 Q So you think it's -- where they're 2 saying their defining their analysis to the 12 3 authorities cited in the Citizen Petition, that 4 they should ignore that and then just start adding 5 other studies. Is that what you're saying?</p> <p>6 A Well, if they're specifically stating, 7 In this section we're only going to do those 12 8 studies, okay, fine. I'm not necessarily 9 commenting on that. I'm commenting on the -- on 10 the submission as a whole, and particularly how 11 dose-response is dealt with in their response.</p> <p>12 Q Well, turn the -- turn to page 21 of 13 your -- of the response. In the section Part 4, 14 "Talc and Ovarian Cancer Risk," do you see that 15 section?</p> <p>16 A Yes, I do.</p> <p>17 Q The next section, "Introduction," it 18 says: "Above we reviewed the literature citations 19 including the" --</p> <p>20 THE REPORTER: Excuse me. Can you 21 please start over.</p> <p>22 BY MR. HEGARTY:</p> <p>23 Q "Above we reviewed the literature 24 citations, including the petition of the FDA by 25 I. Epstein, et al."</p> |

April Zambelli-Weiner, Ph.D.

| Page 355 | Page 357 |
|--|--|
| <p>1 Do you see where I'm reading?</p> <p>2 A Yes.</p> <p>3 Q That did not include Harlow, did it?</p> <p>4 A Well, I'm taking your word for it. I 5 haven't gone back and looked at this, so I'll -- 6 I'll assume your -- your premise.</p> <p>7 Q Well, you just looked at the Citizen 8 Petition. It didn't include Harlow, did it?</p> <p>9 A Right, but now we're looking at the PCPC 10 report.</p> <p>11 Q The next sentence says: "The petition 12 cites similar relevant literature published since 13 1995."</p> <p>14 Do you see that?</p> <p>15 A Yes.</p> <p>16 Q So they're limiting their database 17 search to post-1995 studies thereafter, right?</p> <p>18 MR. TISI: Well, why don't you read the 19 paragraph.</p> <p>20 THE WITNESS: Let me just take a moment 21 (Peruses document.)</p> <p>22 Okay. So --</p> <p>23 BY MR. HEGARTY:</p> <p>24 Q So if they did limit their search 25 thereafter to post-1995 literature, that would not</p> | <p>1 Q Didn't the --</p> <p>2 A It did.</p> <p>3 Q -- 2003 meta-analysis include the Harlow 4 study?</p> <p>5 A Yes, it did.</p> <p>6 Q So what is wrong with the way they laid 7 this out in not including the Harlow study from 8 what they said they did?</p> <p>9 A Again, this is my expert opinion. I 10 am -- I am standing by it, that if you are 11 representing a review of a body of evidence to 12 FDA, you should be fulsome in that -- in that 13 representation. And I think that Harlow should 14 have been included.</p> <p>15 Q You say: "Huncharek and Muscat provided 16 no discussion of Harlow 1992."</p> <p>17 Here they're incorporating what they 18 included in their Huncharek paper. How is that no 19 discussion?</p> <p>20 MR. TISI: Objection.</p> <p>21 THE WITNESS: Again, I'm just going to 22 refer you back and -- you know, I'm trying to 23 answer your questions, but refer you back to the 24 table that, to my knowledge, whether in the PCPC 25 report or otherwise, there is no discussion of the</p> |
| <p>1 include the 1992 Harlow study, correct?</p> <p>2 A Well, I'm not certain. I mean they say: 3 "We searched electronic databases in order to 4 determine if other citations exist that were not 5 cited by Epstein or Huncharek." So they don't 6 really time limit that.</p> <p>7 Q Well, but Huncharek did cite to the 1992 8 Harlow study, didn't it?</p> <p>9 A I believe so. You're bouncing around a 10 lot, so I'm just trying to keep up here.</p> <p>11 Q Well, Doctor, you wrote the report and 12 you should be an expert on your report.</p> <p>13 MR. TISI: Oh, come on, Counsel, that's 14 unfair. You're peppering her with questions, and 15 she needs to go back and see what she's got.</p> <p>16 MR. HEGARTY: Well, the objection --</p> <p>17 MR. TISI: I mean, well, that was a 18 snarky comment, so just ask her questions.</p> <p>19 MR. HEGARTY: Well, I think what's being 20 done here is running out my time.</p> <p>21 MR. TISI: She's not running out the 22 time. You're asking her silly questions.</p> <p>23 MR. HEGARTY: Yes, she is.</p> <p>24 MR. TISI: Go ahead.</p> <p>25 BY MR. HEGARTY:</p> | <p>1 positive dose-response data that exists within 2 this evidence base, and there are two examples of 3 that.</p> <p>4 BY MR. HEGARTY:</p> <p>5 Q Well, that's not true either because 6 they incorporated into their paper the 2003 7 meta-analysis, correct?</p> <p>8 A They incorporate the Harlow paper, but 9 that's different than what I'm saying.</p> <p>10 Q Well, they do make reference to papers 11 that you contend show a positive dose-response by 12 referring to the 2003 meta-analysis, correct?</p> <p>13 MR. TISI: Objection.</p> <p>14 THE WITNESS: We're talking apples and 15 oranges. That's not what I'm referring to.</p> <p>16 BY MR. HEGARTY:</p> <p>17 Q Now, in page -- again, on page 37 under 18 your table, you make statements about what they 19 should have included about dose-response, 20 including positive dose-response data described in 21 individual studies. You say that, correct?</p> <p>22 A I'm sorry, where are you?</p> <p>23 Q In the paragraph below the table, 24 Table VI.</p> <p>25 A Okay.</p> |

April Zambelli-Weiner, Ph.D.

| Page 359 | Page 361 |
|--|--|
| <p>1 Q You say: "The authors do not report the 2 positive dose-response data described in the 3 individual epidemiologic studies." Correct? 4 A Correct. 5 Q And you take issue with that? 6 A That's correct. 7 Q You say that it's wrong for them not to 8 do that, correct? 9 MR. TISI: Objection. 10 THE WITNESS: Well, I think I'll repeat 11 again what -- what I said in prior answers, which 12 is in advocating such a strong position to FDA on 13 dose-response, dose-response as a key tenet of a 14 causal assessment, there's not a fulsome 15 discussion of dose-response. 16 BY MR. HEGARTY: 17 Q Where is it defined in the medical 18 literature what constitutes a strong position in a 19 paper? That's your subjective take, correct? 20 MR. TISI: Objection. 21 THE WITNESS: Again, as an 22 epidemiologist doing this kind of work in the 23 business of submitting -- you know, helping 24 clients submit things to FDA, I would not do this. 25 I would not consider this an appropriate and</p> | <p>1 BY MR. HEGARTY: 2 Q So you would fault an author of a report 3 if they reported on positive dose-response data 4 but did not give equal time to those studies that 5 didn't find a dose-response, correct? 6 MR. TISI: Objection. 7 THE WITNESS: Again, it's -- I would say 8 it's contextually dependent. 9 BY MR. HEGARTY: 10 Q Well -- 11 A You're asking a very just general 12 broad question. 13 Q You're -- you're supposedly the expert. 14 If somebody in a report is advocating that, based 15 on the data in the ovarian cancer case-control 16 studies, there is a dose-response, you would fault 17 that author if they didn't give equal time to the 18 data that didn't show a dose-response, correct? 19 MR. TISI: Objection. 20 THE WITNESS: No. Not -- I'm sorry. 21 MR. TISI: Objection. 22 THE WITNESS: No, not necessarily, and I 23 think you're -- you're mischaracterizing or 24 misunderstanding my -- my position. 25 BY MR. HEGARTY:</p> |
| <p>1 fulsome discussion of an important issue in a 2 causation analysis. That's my opinion. 3 BY MR. HEGARTY: 4 Q Cite me a published authority that -- 5 that supports that opinion. 6 MR. TISI: Objection. 7 THE WITNESS: I'm not even sure what 8 you're asking me. 9 BY MR. HEGARTY: 10 Q Cite me a published authority that 11 defines what it -- what it takes in a paper to be 12 a strong position. That's your subjective view, 13 correct? 14 A Well, I -- 15 MR. TISI: Objection. 16 THE WITNESS: I think the repeated 17 statements, and we could -- we could certainly, 18 you know, if you wanted to spend the time, go 19 through all of them and pull them out where they 20 complete -- sorry, repeatedly rely upon the 21 assertion that there's no evidence of a 22 dose-response, that an inverse dose-response is 23 evidence against a causal assessment. They're 24 clearly arguing for that position. That's clearly 25 the position that they're taking and advocating.</p> | <p>1 Q So you would think in some instances if 2 an author advocates that there is a dose-response, 3 and they ignored data that didn't show a 4 dose-response, that's okay? 5 MR. TISI: Objection. 6 THE WITNESS: Again, I think I said it's 7 contextually dependent. It's dependent upon the 8 body of literature. It's dependent upon what -- 9 you know, there's a tenet in epidemiology that you 10 can't prove the null hypothesis. So even the 11 concept of data against a dose-response is sort of 12 erroneous. 13 So, again, I'm just going to say 14 generally that it would be contextually dependent 15 on what that data was and how it was treated, and 16 I would have to make that evaluation on a case-by- 17 case basis. 18 BY MR. HEGARTY: 19 Q Is there data in the ovarian cancer 20 literature against a dose-response? 21 A That's a very vague question, and, you 22 know, I probably should have started with this way 23 back when we started talking about dose-response 24 that I'm just taking the assumption that you're 25 talking about a linear dose-response because there</p> |

April Zambelli-Weiner, Ph.D.

| Page 363 | Page 365 |
|--|---|
| <p>1 are a lot of different types of dose-response -- 2 dose responses. So it's a very complex question. 3 I'm not really sure exactly.</p> <p>4 Q Well, did -- did you analyze all the 5 dose-response data from the case-control studies 6 and the cohort studies in the ovarian cancer 7 literature?</p> <p>8 A No. That wasn't -- that wasn't my 9 charge.</p> <p>10 Q Well, then, how can you say that the 11 authors did not report on positive dose-response 12 data if you didn't analyze all the studies?</p> <p>13 A Because I became aware of that data. So 14 certainly I'm aware that that data exists in my 15 review of the --</p> <p>16 THE REPORTER: Aware that that data?</p> <p>17 BY MR. HEGARTY:</p> <p>18 Q Okay. You don't --</p> <p>19 THE REPORTER: I couldn't hear -- excuse 20 me. I need -- I could not hear. There was a 21 cough and I couldn't hear.</p> <p>22 MR. TISI: I think she said --</p> <p>23 THE REPORTER: "So certainly I'm aware 24 that that data" --</p> <p>25 MR. TISI: I think she said "exists,"</p> | <p>1 reflect as to the propriety of that response. 2 BY MR. HEGARTY: 3 Q My question is, in that paragraph, do 4 you cite any studies that report a positive 5 dose-response from the data? 6 A I don't know what paragraph you're 7 referring to. 8 Q It's the paragraph we've been talking 9 about, the paragraph under the table. 10 A Well, I think the table cites to two 11 studies. So I'm not really sure what you're 12 asking me. 13 Q Doctor, please listen to my question. 14 My question is, in the paragraph I'm 15 looking at under the table -- 16 A Mm-hmm. 17 Q -- do you cite to any study reporting a 18 positive dose-response from the data? 19 A There's no citations in that paragraph, 20 but that doesn't mean I'm not citing studies that 21 have positive dose-response data. 22 Q Okay. 23 A So I'm not really sure why you're asking 24 me that. 25 Q What study on that -- on that page has a</p> |
| Page 364 | Page 366 |
| <p>1 and then I -- went off the record. 2 BY MR. HEGARTY: 3 Q You made no reference in that section to 4 what data -- to the data to which you're referring 5 to, correct? In other words, you make no 6 response -- no citation to any literature that 7 shows a positive dose-response data in that 8 paragraph, correct?</p> <p>9 MR. TISI: Objection. She cites Harlow. 10 MR. HEGARTY: Chris, do you want to take 11 the microphone and answer for her? 12 MR. TISI: I -- I'd love -- I'd love to, 13 but you've got to ask the question. She just 14 testified to Harlow. 15 MR. HEGARTY: Chris, please stick to the 16 obligations that you committed to under the 17 court's order -- 18 MR. TISI: I got it, but, you know, 19 you -- 20 MR. HEGARTY: -- and stick to the form 21 objections. 22 MR. TISI: You're peppering questions 23 and not allowing her to answer, and then running 24 over -- running over things. 25 MR. HEGARTY: Well, we'll let the record</p> | <p>1 positive -- has positive dose-response data? 2 A Chang and Harlow. 3 Q Okay. And you've analyzed that data, 4 and it's your opinion that that data shows a dose- 5 response; is that correct? 6 A It's my opinion that the authors report 7 positive dose-response data, yes. 8 Q Now, that's not my question. My 9 question is, in your opinion, does the data show a 10 positive dose-response from your own independent 11 analysis? 12 A I do not -- I did not do an, excuse me, 13 independent analysis of dose-response. That 14 wasn't my charge. It was a critical review of 15 these works, and that's what my review is focused 16 on. 17 Q Over on page 37 under the section 18 "Contradictory unsupported claims of uncontrolled 19 confounding," you make the statement that -- over 20 on -- turning to page 38 of that section. The 21 paragraph which begins "On page 4." Do you see 22 that paragraph? 23 A Yes, I do. 24 Q "They further discuss this on 25 page 23" -- this is the second line -- "where they</p> |

April Zambelli-Weiner, Ph.D.

| Page 367 | Page 369 |
|---|---|
| <p>1 cite an article by Rosenblatt and colleagues as 2 empirical data supporting their assertion that 3 smoking is an important confounder." 4 Do you see where I'm reading? 5 A Yes, I do. 6 Q Nowhere in this response do they ever 7 say that smoking is an important confounder, do 8 they? 9 A Well, I would have to go back and look 10 at the specific language they use. 11 Q Well, go over to page 23 of the 12 response. Second paragraph. This is where they 13 talk about Rosenblatt. Nowhere in that 14 paragraph -- and you read the response -- or 15 anywhere in this report do they ever say that 16 smoking is an important confounder, do they? 17 A Well, again, without rereading this 18 entire report, which I know we -- none of us want 19 to do, I'll say in that paragraph they -- they 20 say: "An example of a factor that could confound 21 the weak effect shown for perineal talc is 22 smoking." So they're -- they're calling out 23 smoking as a confounder. "It's now recognized," 24 and they go on to talk about -- about that. 25 Q The word "important" is your word,</p> | <p>1 A I don't know what your question is. 2 Q Well, the statement that they make there 3 that says that "Rosenblatt reported that smokers 4 are more likely to engage in perineal talc dusting 5 compared with nonsmokers" is a true statement, 6 isn't it? 7 A I don't know. We can go back and look 8 at Rosenblatt. 9 (Exhibit No. 23 was marked for 10 identification.) 11 BY MR. HEGARTY: 12 Q Here is Exhibit 23, which is the 13 Rosenblatt studies. If you look in the Abstract 14 section on the first page, the Results section in 15 the middle, they say that smokers -- they say 16 that: "Women who smoke cigarettes or were in 17 highest BMI were more likely to engage in perineal 18 use of powder." Correct? 19 A I'm sorry, I'm just looking (reading to 20 herself) -- yes. 21 Q So what is wrong -- what is wrong with 22 their statement in the second paragraph on page 23 23 about what they say concerning the Rosenblatt 24 study? 25 A You're back on the PCPC report?</p> |
| <p>1 correct? 2 A I'm sorry. We're back on -- 3 Q The word in the report that I read to 4 you, the word "important" is your word. It's not 5 the word in their response, is it? 6 A I'm just trying to find it. 7 I don't know. The answer is I'm not 8 sure if they've ever used the word "important" to 9 describe smoking as a confounder. 10 Q Okay. You also cite in that part of the 11 report, this is the paragraph on page 38 beginning 12 on page 4, that they -- they referred to a finding 13 of in Rosenblatt of 1.2. Do you see where I'm 14 reading? 15 A Yes. 16 Q Nowhere in this paper do they ever make 17 reference to the 1.2 odds ratio that Rosenblatt 18 reports, do they? 19 A Well, they -- they don't cite the 1.2, 20 but they -- they do refer to Rosenblatt, that 21 smokers are more likely to engage in talc dusting. 22 So, I mean, obviously you can go back to the paper 23 and -- and pull that data. 24 Q Well, that -- that's a true statement 25 from Rosenblatt, isn't it?</p> | <p>1 Q Yes. 2 A Okay. I'm going to go back to my report 3 for a minute. (Peruses document.) 4 So I -- I think the point that I'm 5 making is I'm not necessarily disagreeing with the 6 characterization of -- of the odds ratio. I think 7 that I'm making a different point here. 8 Q And you're making a point that they 9 don't make in their response, do you -- or do 10 they? 11 A I'm losing your -- your train of -- the 12 line of questioning. 13 Q Well, you're making a point about how 14 they're making reference to Rosenblatt that they 15 don't do in their response. Do they? 16 A Can we -- could we just slow it down for 17 a minute? Because you have me bouncing between 18 things and I'm getting confused. So if it's okay, 19 I would just like to take a minute and reorient 20 myself to my report. 21 Q How much time do you need? 22 A I don't know. A minute. I mean -- 23 Q Well, I'm not -- we'll take -- 24 MR. TISI: We can do that for the 25 record.</p> |

April Zambelli-Weiner, Ph.D.

| Page 371 | Page 373 |
|--|--|
| <p>1 MR. HEGARTY: Go off the record, please. 2 MR. TISI: Just for a minute is fine. 3 THE VIDEOGRAPHER: The time is 4 1:49 p.m., and we're going off the record. 5 (Pause in the proceedings.) 6 THE VIDEOGRAPHER: The time is 1:51 7 p.m., and we're back on the record. 8 BY MR. HEGARTY: 9 Q Doctor, we went off the record for a 10 moment to allow you to look at the Rosenblatt 11 study and compare it to your study, and let me go 12 back to -- I think the point I was trying to make 13 is that you make the assertion in your report that 14 Huncharek and Muscat claim a positive significant 15 association from the Rosenblatt data for a 16 relative risk of 1.2 that is not statistically 17 significant. 18 Nowhere in the response do they make 19 that point, do they? 20 A They don't specifically call out that 21 point, but I'm citing the data in Rosenblatt that 22 supports the point. So I think, you know, I'm 23 trying to make two points. I'm making the point 24 that they're relying on data that is not 25 statistically significant here in this regard, and</p> | <p>1 Q That's -- that's a misstatement, isn't 2 it? 3 A We could look at -- look it up. 4 Q Well, is it your testimony that the -- 5 that the meta-analysis of hospital-based controls 6 showed a 19 percent increased risk of ovarian 7 cancer for talc-exposed patients? 8 A I would have to go back and review that. 9 Q Well, where did that 19 percent number 10 come from? 11 A Again, I'd have to go back and look just 12 to make sure that that's -- that that's accurate. 13 But... 14 Q You've got to go back to where? 15 A The subgroup analysis. 16 Q Well, if you look at Exhibit 16, that's 17 the 2003 paper, the Huncharek meta-analysis. Do 18 you have that document? 19 A Yes. 20 Q If you look over at page 1959, the 21 paragraph beginning "Table 1 on the left-hand 22 column" -- do you see that paragraph? 23 A Yes. "As seen in Table 1" or "Table 1"?24 Q The paragraph beginning "Table 1 shows." 25 A Mm-hmm, yes.</p> |
| <p>1 relying on what they would call modest risk 2 estimates that, you know, or weak -- weak effects 3 to support the notion that smoking may be 4 confounding the association between talc and 5 ovarian cancer, wherein other parts of their 6 report and of their papers they dismiss similar -- 7 similar odds ratios, both in magnitude but also 8 with regard to statistical significance. 9 Q If you turn over to page 39 of your 10 report. In the second paragraph on that page 11 beginning "A similar position" -- do you see where 12 I'm reading? 13 A Yes. 14 Q About two-thirds of the way down, you 15 state that: "As example on page 20" -- do you see 16 where I'm reading? 17 A Yes. 18 Q "As example on page 20 of the 2009 H&M 19 report, the authors claim the findings of their 20 subgroup meta-analysis of hospital-based controls 21 showed no increased risk, when it actually showed 22 a 19 percent increase risk of ovarian cancer for 23 talc exposed patients." 24 Do you see where I'm reading? 25 A Yes, I do.</p> | <p>1 Q Do you see where I'm reading? 2 A Yes. 3 Q About two-thirds of the way down it 4 says: "Interestingly, pooling all hospital-based 5 studies" -- do you see where I'm reading? 6 A I do. 7 Q -- "yielded a relative risk of 1.19, 8 0.99 to 1.4." Do you see where I'm reading? 9 A Yes, I do. 10 Q Is that where you got the 19 percent 11 number from? 12 A Yes, I believe so. 13 Q That number is not statistically 14 significant, is it? 15 A It is not statistically significant, 16 that's correct. 17 Q And includes -- it includes the null 18 value, correct? 19 A Correct, but that is not interpret -- 20 that is not appropriate to interpret that as no 21 association or no increased risk. 22 Q Doctor, listen to my question. Does the 23 confidence interval I read to you include the null 24 value? 25 A Yes, it does.</p> |

April Zambelli-Weiner, Ph.D.

| Page 375 | Page 377 |
|---|---|
| <p>1 Q Including the null value means you 2 cannot rules that that number is not due to 3 chance, correct? 4 ^Ck MS. PARFITT: Objection. 5 THE WITNESS: It's a loose -- a loose 6 interpretation of it. But, again, I'm making the 7 distinction -- this entire section is actually -- 8 and there's another section in my report -- making 9 the distinction between statistical significance 10 and the magnitude of the risk estimate. 11 BY MR. HEGARTY: 12 Q Please listen -- 13 A They're not the same thing. 14 Q Please listen to my question. I just 15 want an answer to this question: Including the 16 null value in a confidence interval means that you 17 cannot conclude that that number is not due to 18 chance, correct? 19 MR. TISI: Objection. 20 THE WITNESS: I -- I don't agree with 21 your -- with your characterization. 22 BY MR. HEGARTY: 23 Q Okay. Including the null value in a 24 confidence interval means that the study shows no 25 association between the exposure and the disease</p> | <p>1 A 0.99 to 1.41. 2 Q And you think that it's okay if you 3 report the confidence intervals to -- to say that 4 if it's not statistically significant, that study 5 does show an increased risk of 19 percent. 6 MR. TISI: Objection. 7 THE WITNESS: Absolutely. The 8 definition of a positive association is a risk 9 estimate greater than 1.0. Moise Desvarieux, 10 Epidemiology 101. Look it up. 11 BY MR. HEGARTY: 12 Q What is the reference? 13 A Desvarieux. 14 Q If a confidence interval includes 1.0, 15 that is compatible with no difference being a 16 likely explanation, correct? 17 A It's within the range of likely values. 18 Q Doctor, you have actually testified in 19 the past that if a confidence interval includes 20 1.0, that is compatible with no difference being a 21 likely explanation. Correct? 22 A I think I just -- I think I just said 23 that. I said it's within the range of likely 24 values. But what -- but important caveat, they're 25 not all as likely. They're not equally likely.</p> |
| <p>1 that's being studied, correct? 2 MR. TISI: Objection. 3 THE WITNESS: No, I don't agree with 4 that. 5 BY MR. HEGARTY: 6 Q So you would -- and you -- strike that. 7 And is it your testimony that in this 8 instance, the 19 percent number that is -- that I 9 referenced from the 2003 paper with the confidence 10 interval that includes 1.0, shows a 19 percent 11 increased risk of ovarian cancer for talc-exposed 12 patients? 13 A Absolutely. Textbook epidemiology. 14 Q Okay. Even though it's not 15 statistically significant. 16 A Absolutely. Those are two entirely 17 different concepts. 18 Q Certainly to say it shows a 19 percent 19 increased risk without saying it's not 20 statistically significant is misleading, isn't it? 21 A Not necessarily, if you report the 22 confidence intervals. 23 Q Did you report the confidence intervals? 24 A Yes. 25 Q And what did you report them as?</p> | <p>1 Q Meaning that it is compatible with no 2 difference between cases and controls. That's 3 what that means, correct? 4 A I would not characterize it that way. 5 Q So you disagree with the way I 6 characterize it; is that correct? 7 A Can you read back your question? 8 Q Sure. A confidence interval that 9 includes 1.0 is compatible with no difference 10 between cases and controls, correct? 11 MR. TISI: Objection. 12 THE WITNESS: I think that that is a 13 likely value. It is within the range of likely 14 values. Again, with the caveat that they are 15 not -- all the -- all the values within a 16 confidence interval are not equally likely. 17 But, yes, I mean it is compatible with 18 no association as a likely value based on the 19 underlying data. But, again, an important caveat, 20 just to be accurate, if, for example, in this case 21 when you have a confidence interval that goes 22 to .99, that's the limit of the confidence 23 interval, and that is actually the least likely 24 value. So it's really important to understand 25 that not all values within a confidence interval</p> |

April Zambelli-Weiner, Ph.D.

| Page 379 | Page 381 |
|---|---|
| <p>1 are equally likely. 2 BY MR. HEGARTY: 3 Q Nor is it proper to say that the point 4 estimate in a nonstatistically significant finding 5 is the most likely value, as you say on page 41. 6 That's not right, is it? 7 A That is correct actually. The point 8 estimate is always the most likely estimate of the 9 true population parameter given the data. 10 Q Cite for me an authority that supports 11 that statement. 12 A I -- I would refer you to epidemiology 13 biostatistics textbooks again. 14 Q Which textbook? 15 A I don't know specifically. I've given 16 you Rothman. It may be in there. 17 Q Well, cite for me an authority that you 18 are aware of that says that the point estimate in 19 a nonstatistically significant finding is the most 20 likely value. 21 MR. TISI: Objection. 22 THE WITNESS: I think I answered your 23 question. 24 BY MR. HEGARTY: 25 Q What is the authority?</p> | <p>1 value of 1.0, based on an alpha value of 0.05, you 2 can't reject the null hypothesis of that 3 difference, that's correct. 4 THE WITNESS: Could I take a quick 5 break? 6 MR. HEGARTY: Sure. 7 THE WITNESS: Thank you. 8 MR. HEGARTY: Let's go off the record. 9 THE VIDEOGRAPHER: The time is 2:01 p.m. 10 We're going off the record. (Recess.) 12 THE VIDEOGRAPHER: The time is 2:05 p.m. 13 We're back on the record. 14 BY MR. HEGARTY: 15 Q Doctor, we're on page 39 of your report. 16 A Okay. 17 Q Are you there? 18 A Yes. 19 Q If you look towards the bottom, the 20 paragraph beginning with the word "Further." Do 21 you see that? 22 A Yes. 23 Q About three lines down from the 24 beginning of that paragraph, over to the right-hand column, you say: "Unfortunately, the</p> |
| Page 380 | Page 382 |
| <p>1 A I think I said -- again, I'm not citing 2 a specific authority, but I've given you numerous 3 textbook authorities to support my expertise as an 4 epidemiologist. 5 Q Cite for me anything besides the Rothman 6 text. 7 A I'm not sure. I'm sure I could find 8 something for you if you're really interested. 9 Q When you have a nonstatistically 10 significant finding, the null hypothesis has not 11 been disproved, correct? 12 MR. TISI: Objection. 13 THE WITNESS: I'm sorry, that's a 14 convoluted question. Can you repeat, please? 15 BY MR. HEGARTY: 16 Q Sure. When you have a nonstatistically 17 (sic) finding between an exposure and a disease, 18 then the null hypothesis has not been disproved, 19 correct? 20 A I'm not sure -- your wording is throwing 21 me off. Do you want to reword that or -- 22 Q No. Can you not answer my question? 23 A Let me take a look. (Peruses monitor.) 24 Right, you cannot -- if -- if the 95 25 percent confidence interval includes the null</p> | <p>1 authors unevenly discuss the evidence base only 2 citing studies that support the case for a 3 noncausal relationship and utilizing the observed 4 differences -- difference in risk estimates 5 between population and hospital-based case-control 6 studies as evidence undermining the causal 7 association, et cetera." 8 Do you see where I'm reading? 9 A I do. 10 Q Is it your testimony or your opinion by 11 that statement that in the response that they -- 12 that the authors only cited to studies that 13 support the case for a noncausal relationship? Is 14 that what you're saying there? 15 A No, I don't think that that accurately 16 characterizes what I'm saying there. 17 Q Well, tell me how my reading is not 18 accurate. 19 A Well, the section is specifically around 20 the selection bias issue and the issue related to 21 hospital- versus -- versus population-based 22 controls. So I think this gets to something we 23 discussed earlier, which is the lack of a fulsome 24 discussion around this issue, and reasons why you 25 might observe the differences that were -- were in</p> |

April Zambelli-Weiner, Ph.D.

| Page 383 | Page 385 |
|---|--|
| <p>1 observed the meta-analysis. 2 Q So is it your testimony that the 3 sentence I read only concerns the issue of 4 selection bias as it relates to the hospital- and 5 population-based case-control studies? It's not 6 an issue generally as to the causal relationship 7 across the studies? 8 MR. TISI: Objection. 9 THE WITNESS: Well, I think I -- I'm 10 citing it here in that section specifically. So, 11 yeah, here it is there to reference that 12 particular issue in that -- that section. 13 BY MR. HEGARTY: 14 Q So you're not saying that the authors of 15 the 2009 response only cited studies that support 16 the case for a noncausal relationship between talc 17 and ovarian cancer. That's not what you're 18 saying, correct? 19 MR. TISI: Objection. 20 THE WITNESS: Let me read back your 21 question. (Peruses monitor.) 22 That's -- that's not what I'm saying in 23 this section. I mean I'm not really commenting on 24 that in terms of the breadth of their causation 25 analysis, but this statement relates to the issue</p> | <p>1 appraisal of -- of these studies. And so 2 particularly related to the dose-response data and 3 the -- you know, uncontrolled confounding and 4 other issues that are then proffered in the 2009 5 report as evidence against a causal association. 6 So I think that, again, I'm trying to 7 answer your question. I mean I think certainly 8 there is -- well, you know, I'm just -- I'm not 9 even sure I can answer that question. Do you want 10 to try rephrasing it? I'm -- it's confusing. 11 Q What part -- I'm not sure what part is 12 confusing. Where in your paper do you put forth 13 any valid data or analysis from the two papers or 14 the response? Do you do that anywhere? 15 A Well, certainly there's citations in 16 here. If this is what you're asking -- again, I'm 17 not -- I'm not sure what you're asking. If you're 18 asking if I'm citing to studies that have valid 19 data in them, sure. 20 Q No, I'm citing to what you said you were 21 going to do. Where in your report do you identify 22 the valid data and analysis that the authors set 23 out in the 2003 and 2007 studies and the 2009 24 response? 25 A Again, as part of -- so let's back up to</p> |
| <p style="text-align: center;">Page 384</p> <p>1 of selection bias. 2 BY MR. HEGARTY: 3 Q At the beginning of the deposition we 4 talked about what you're -- you were doing in this 5 paper, and there -- in this -- in your analysis, 6 and on page 9, you -- you said that you were asked 7 to review and assess the validity of the data in 8 claims put forward by Dr. Huncharek and 9 Dr. Muscat. 10 Where in your report do you discuss any 11 valid data that they included in their response or 12 their 2003 paper or their 2007 paper? 13 MR. TISI: Objection. 14 THE WITNESS: I'm sorry, can you repeat 15 the question? 16 BY MR. HEGARTY: 17 Q Where in your report do you identify any 18 valid data or assessment of the data that were put 19 forth in the 2003 and 2007 articles and the 2009 20 response? 21 A That's kind of a confusing question, but 22 I'll do my best to answer it. 23 So, again, you asked me initially back 24 in the first session, you know, what my 25 methodology was, and I described it as a critical</p> | <p style="text-align: center;">Page 386</p> <p>1 what the methodology is to -- I'm trying to answer 2 your question fully. 3 It's an assessment of the internal 4 validity of these studies. So my analysis of 5 these studies is that they have very low validity 6 overall, both of these studies. So that's the -- 7 that's the focus of my report and that's what I'm 8 describing in my report is my analysis of the 9 internal validity of these studies, which is very 10 low. 11 If I was asked to do a causation 12 analysis or weight of evidence analysis or submit 13 something to FDA, I would give these studies very 14 little, if any, weight whatsoever, and would not 15 trot them into FDA ever. So that's the focus 16 of -- that's the focus of my -- of my report. 17 Q You're not answering my question. 18 My question was, point to me in your 19 report where you set out the valid analysis and 20 the valid data that the -- the articles reported 21 and the response reported? 22 MR. TISI: Objection. Asked and 23 answered. 24 THE WITNESS: Again, I feel like I 25 answered your question. That was not my task. My</p> |

April Zambelli-Weiner, Ph.D.

| Page 387 | Page 389 |
|--|--|
| <p>1 task was to assess the internal validity of these 2 studies. I did that, and I reported out on that 3 in my report. 4 BY MR. HEGARTY: 5 Q If you look over on page 40 of your 6 report, you say in the middle of that page, the 7 paragraph beginning "On page 19" -- do you see 8 that? 9 A "On page 19," yes. 10 Q You report what the Huncharek and Muscat 11 articles say, and then you say that statement is 12 incorrect, and the statement of fact by the 13 Epstein authors is correct. 14 Do you see where I'm reading? 15 A Well, yeah, I'm just taking a look at 16 it. (Peruses document.) 17 Q How is the statement by Huncharek and 18 Muscat -- by Huncharek -- first of all, let me 19 back up. 20 You say that Huncharek and Muscat make 21 that statement. Muscat again was not an author of 22 that paper, did he -- was he? 23 MR. TISI: Objection. Asked and 24 answered. About ten times. 25 THE WITNESS: Again, I believe we're</p> | <p>1 BY MR. HEGARTY: 2 Q Correct? 3 MR. TISI: Objection. 4 THE WITNESS: Are you -- are you 5 referring to the 2003 paper? 6 BY MR. HEGARTY: 7 Q Yes. 8 A I don't recall exactly if they laid it 9 out that way, but I -- it is my understanding that 10 they did a causation analysis, yes. 11 Q And they concluded after that analysis 12 that the available observational data do not 13 support the existence of a causal relationship 14 between perineal talc exposure and an increased 15 risk of epithelial ovarian cancer. That was their 16 conclusion, correct? 17 A Well, I think in a way you're exactly 18 illustrating my point, which is sort of the point 19 of this section, is the conflation of 20 epidemiologic concepts. Because a meta-analysis 21 is simply a statistical analysis. By itself, it 22 cannot prove or disprove causation. So to make 23 the leap from a statistical finding to causation 24 is -- is inappropriate. 25 Q Well, it's -- you can do that if you do</p> |
| Page 388 | Page 390 |
| <p>1 talking here about the PCPC report, which he is an 2 author on. But I've also addressed previously his 3 association with the data that shows up in the 4 2003 paper. 5 BY MR. HEGARTY: 6 Q Okay. You note that what Epstein 7 reports, he -- the -- the part of the report 8 they're referring to there is Epstein claiming 9 that the Huncharek study supports an association 10 between perineal talc dusting and ovarian cancer 11 risk. That's what you're saying there, right? 12 A Let me -- let me -- let me tell you what 13 I'm saying. Hopefully that will answer your 14 question. 15 When a -- when the PCPC report says that 16 the petitioners erroneously indicate that the 17 meta-analysis supports an association, that's the 18 part that I'm objecting to. The meta-analysis as 19 reported shows a 1.33 pooled risk estimate. So 20 that is by definition a positive association. 21 Q But you're aware, Doctor, that the 22 authors from the 2003 paper did more than just 23 report the odds ratios. They, in essence, did a 24 Bradford Hill analysis. 25 MR. TISI: Objection.</p> | <p>1 a Bradford Hill analysis, can't you? 2 A But that's not what we're talking about. 3 Right now we're talking about the results of the 4 meta-analysis. 5 Q We're talking about what their analysis 6 was in their paper and their conclusions that they 7 drew from that paper, correct? 8 A Well, we started this line of 9 questioning with you pointing me to this 10 statement, which says: "The petitioners 11 erroneously indicate that the meta-analysis 12 supports an association." 13 So I'm responding to that specific 14 comment and saying that is an inappropriate 15 characterization of the results of meta-analysis. 16 Q All the response is doing is reporting 17 what the authors said from the 2003 paper. 18 Isn't -- aren't they? 19 A I -- I don't know what you're asking me. 20 I'm sorry. 21 Q Well, they reported what the authors 22 said, which from their review of the data, it did 23 not support a causal relationship. That's what 24 the 2009 response says, correct? 25 A Are -- are we still here or are we</p> |

April Zambelli-Weiner, Ph.D.

| Page 391 | Page 393 |
|---|--|
| <p>1 somewhere else now?</p> <p>2 Q We're still here.</p> <p>3 A So we're talking about the</p> <p>4 meta-analysis. We're talking about the statement</p> <p>5 being incorrect.</p> <p>6 Q The statement --</p> <p>7 A Are we talking about something</p> <p>8 different?</p> <p>9 Q They didn't report an inaccurate</p> <p>10 statement from the 2003 meta-analysis, correct?</p> <p>11 A Who is "they"?</p> <p>12 Q Drs. Muscat and Huncharek.</p> <p>13 A Okay. Hopefully you understand why this</p> <p>14 is confusing. We're starting with a comment made</p> <p>15 by Epstein. We have Huncharek and Muscat in the</p> <p>16 PCPC report responding to their comment, calling</p> <p>17 their comment inappropriate. And I'm responding</p> <p>18 to their comment, to Huncharek and Muscat's</p> <p>19 comment.</p> <p>20 Q That's not my question. My question is</p> <p>21 simply, in the 2009 response, they accurately</p> <p>22 reported what the authors concluded from the 2003</p> <p>23 study, correct?</p> <p>24 A I -- I can't just blanketly agree with</p> <p>25 that. I'm not even sure what you're asking.</p> | <p>1 MS. PARFITT: Objection.</p> <p>2 MR. HEGARTY: Can -- can we limit it to</p> <p>3 one person objecting?</p> <p>4 MS. PARFITT: Sure. But I get excited</p> <p>5 every now and then. I just want to join in.</p> <p>6 MR. HEGARTY: I got it.</p> <p>7 BY MR. HEGARTY:</p> <p>8 Q Okay. Can you answer my question?</p> <p>9 A Can you repeat it, please?</p> <p>10 Q So it would be -- so in your opinion, it</p> <p>11 would be improper in any meta-analysis to draw a</p> <p>12 causal conclusion from the results, correct?</p> <p>13 MR. TISI: I got it. Objection.</p> <p>14 THE WITNESS: I think it's a very broad</p> <p>15 question. I would have to -- I'd have to see the</p> <p>16 context. I don't know if you're asking me if</p> <p>17 within the context of a meta-analysis you can do a</p> <p>18 causal assessment, but I'm sure that that could</p> <p>19 be -- that could be done.</p> <p>20 I think what I'm saying is that to infer</p> <p>21 that a single data point or a single study proves</p> <p>22 or disproves causation is not -- is not</p> <p>23 appropriate.</p> <p>24 BY MR. HEGARTY:</p> <p>25 Q You just testified, and I rolled back to</p> |
| <p>1 Q Well, they reported that the 2003 study</p> <p>2 did not support the existence of a causal</p> <p>3 relationship, and that's what the authors said,</p> <p>4 correct?</p> <p>5 A Well, that's an incorrect statement.</p> <p>6 That's an incorrect -- that is not a</p> <p>7 scientifically defensible assertion. You cannot</p> <p>8 make the leap from the results of a statistical</p> <p>9 analysis to causation. You can't say that a</p> <p>10 meta-analysis does not support causation. That's</p> <p>11 not appropriate.</p> <p>12 Q Okay. Cite for me authority that says</p> <p>13 that.</p> <p>14 A Any authority that talks about Bradford</p> <p>15 Hill, that talks about causation -- I mean we all</p> <p>16 know what a causation analysis is, hopefully, but</p> <p>17 we can go through that. I mean it's the</p> <p>18 evaluation of different lines of evidence to</p> <p>19 address a question. One single data point cannot</p> <p>20 address causation. A single meta-analysis cannot</p> <p>21 address causation.</p> <p>22 Q So in your opinion, it would be improper</p> <p>23 in any meta-analysis to draw a causal conclusion</p> <p>24 from the results, correct?</p> <p>25 MR. TISI: Objection.</p> | <p>1 your -- your testimony, that you can't say that a</p> <p>2 meta-analysis does not support causation. The</p> <p>3 reverse would be true as well: You can't say that</p> <p>4 a meta-analysis supports causation, correct?</p> <p>5 MR. TISI: Objection.</p> <p>6 THE WITNESS: Let me read -- let me read</p> <p>7 your question, please. (Peruses monitor.)</p> <p>8 So maybe there's a misunderstanding.</p> <p>9 Let me -- let me try restating just to be clear.</p> <p>10 You can't draw a causal conclusion from</p> <p>11 a single data point from a statistical analysis.</p> <p>12 That's not to say that a meta-analysis can't</p> <p>13 support a causal assessment. That can happen.</p> <p>14 BY MR. HEGARTY:</p> <p>15 Q But in the meta-analysis itself where</p> <p>16 the authors draw from the data -- a single data</p> <p>17 point, it would be improper, according to you, to</p> <p>18 draw the conclusion that it either supports or it</p> <p>19 doesn't support a causal relationship, correct?</p> <p>20 MR. TISI: Objection.</p> <p>21 THE WITNESS: Again, with the caveat --</p> <p>22 I would say, yes, with the caveat that it depends</p> <p>23 on how that's said. It depends if you're saying</p> <p>24 the meta-analysis is, you know, one line of</p> <p>25 evidence in support of a causation or if you're</p> |

April Zambelli-Weiner, Ph.D.

| Page 395 | Page 397 |
|---|---|
| <p>1 saying from this meta-analysis, we cannot infer 2 causation. Those are actually two different 3 things. 4 BY MR. HEGARTY: 5 Q And the latter would be improper, 6 according to you, correct? 7 MR. TISI: Objection. 8 THE WITNESS: Again, yes, I would say -- 9 I just want to be clear because this has been like 10 a very confusing line of questioning -- that it 11 would be inappropriate in my opinion to draw a 12 causal assessment based on the results of a single 13 statistical analysis like a meta-analysis. That's 14 not to say that it can't contribute. That's not 15 to say that a meta-analysis paper doesn't do a 16 broader causal assessment. So there's -- there's 17 a lot of context to that question. 18 BY MR. HEGARTY: 19 Q If you'd turn over to page 41 of your 20 report, please. 21 You cite a portion of the PCPC report on 22 that page beginning with "Two meta-analyses" -- do 23 you see that? 24 A Yes. 25 Q And you say that: "The report says that</p> | <p>1 that's what I wouldn't do. That that's not 2 something that I would do. 3 Q What's not something that you would do? 4 A Jump from a nonstatistically significant 5 finding to a causal assessment. Those are two 6 entirely different things. 7 Q But you're saying that an odds ratio as 8 reported here does show an association. That is, 9 a 0.99 to 1.4 with an odds ratio of 1.99 does show 10 an association. 11 A Absolutely correct, that's a positive 12 association. 13 Q Is it your opinion that the -- that the 14 finding of 1.19 with a confidence interval of 0.99 15 to 1.4 shows an association between talc use and 16 ovarian cancer in the hospital-based studies? 17 A Yes, I would interpret that odds ratio 18 as a 19 percent increased risk. 19 Q And is it your contention that such a 20 conclusion has been generally accepted in the 21 epidemiologic community? 22 A Sure. Absolutely. I mean, I think 23 there's a lot of -- a lot that's been written 24 about certainly the difference between the 25 magnitude of an estimate and statistical</p> |
| Page 396 | Page 398 |
| <p>1 both showed significant differences in summary 2 odds ratios between population-based and 3 hospital-based case-control studies, with the 4 latter showing generally no results." You then go 5 and say: "That statement is false." 6 What is false about that statement? 7 A I think again I'm -- if you will read 8 further down, I'm referring to the subgroup 9 analysis of the 1.19 odds ratio, and that that is 10 not a null finding. 11 Q Okay, so I want to make it clear. 12 It's your testimony that the odds 13 ratio -- an odds ratio of 1.19 with a confidence 14 interval of 0.99 to 1.4 is not a null result? 15 A That's correct. That is a positive 16 association by textbook epidemiology. 17 Q Okay. Cite for me a textbook that says 18 that. 19 A I did. Moise Desvarieux. 20 Q Cite for me where it's been generally 21 accepted that you can conclude with a 22 nonstatistically significant finding that there's 23 a causal association from the -- between the 24 exposure and the disease. 25 A I think I just testified that -- that</p> | <p>1 significance and hypothesis testing. 2 And, you know, even the American 3 Statistical Association recently came out with a 4 whole diatribe on how, you know, we need to get 5 away from the overreliance on -- on statistical 6 significance. So, I think absolutely. These are 7 two entirely different concepts, and, by 8 definition, that's a positive association. 9 Q And you say that the textbook you cite 10 supports that statement. 11 A Yes, it does. 12 Q At the top of page 43 of your report, 13 you say: "The authors assert that weak 14 associations are intrinsically susceptible to 15 bias." 16 That's a true statement, isn't it? 17 A No, I don't -- I don't agree with that. 18 I mean, I think that you have to do an analysis of 19 the study that produced that particular risk 20 estimate. You can have a very modest association 21 that's highly valid and highly reliable and very 22 low risk of bias, and you can have a very elevated 23 risk estimate that's very -- very susceptible to 24 bias or high risk of bias. So I don't think you 25 can just make those kinds of blanket</p> |

April Zambelli-Weiner, Ph.D.

| Page 399 | Page 401 |
|--|--|
| <p>1 characterizations. 2 Q Tell me if you agree with the following 3 statement: "Although lower risks -- lower 4 relative risks can reflect causality, the 5 epidemiologists will scrutinize such associations 6 more closely because there is a greater chance 7 that they are the result of uncontrolled 8 confounding or biases." 9 MR. TISI: Objection. 10 THE WITNESS: I'm just going to read it 11 back, if that's okay. (Peruses monitor.) 12 You know, I -- I think that that's one 13 of those quotes or -- or statements that I 14 think -- I think could be true. I personally take 15 the position that I'm evaluating -- evaluating every 16 study with the same methodology and the same 17 rigor, regardless of what the magnitude of the 18 point estimate is. 19 So I think that, you know, that 20 undertaking of an analysis of internal validity 21 and risk of bias should happen in -- irrespective 22 of what the magnitude of the risk estimate is. 23 BY MR. HEGARTY: 24 Q Tell me if you agree with the following 25 statement: "When considering bias and</p> | <p>1 association in a study, the greater there is 2 for concern -- the greater the concern there is 3 that bias or confounding could be the reason for 4 the association? 5 MR. TISI: Objection. 6 THE WITNESS: Again, I would say -- I 7 think I've said that's contextually dependent. I 8 mean, I would need to look at the body of 9 literature and understand what the risks of bias 10 are. 11 BY MR. HEGARTY: 12 Q Well, bias can explain a finding of a 13 relative risk or an odds ratio of 1.2, correct? 14 MR. TISI: Objection. 15 THE WITNESS: Bias can explain -- I 16 mean, depending upon the nature of the bias, you 17 can have all kinds of effects to -- on the point 18 estimate. So bias can explain a finding of 1.2, 19 of 1.5, of 4.0. You know, it depends again on the 20 specific -- specific study and the specific risks 21 of bias that are -- are at play. 22 BY MR. HEGARTY: 23 Q If you turn over to the Conclusion 24 section on page 45, in the second to last 25 statement -- or the second to the last sentence</p> |
| <p>1 confounders, the weaker the association, the 2 greater the concern that bias or confounding could 3 be the reason for the association." 4 MR. TISI: Objection. 5 THE WITNESS: I'm sure I've seen -- I've 6 seen that written, and I'm sure I can understand 7 why someone would write that. But, again, you 8 know, it really depends upon the question being 9 asked. 10 If we're looking at a body of literature 11 where we have really very little concern about 12 confounding, then I wouldn't be scrutinizing a low 13 or modest relative risk and having extra concern 14 about confounding. So it's very -- it's very 15 contextually dependent. 16 I think the intent there is to say that 17 not knowing anything, you know, and just in a 18 vacuum, if we don't know anything about a 19 particular research question, and we have a more 20 modest relative risk, we want to be sure that we 21 adequately address the risks of bias. But again, 22 I take the position that we should be doing that 23 no matter what. 24 BY MR. HEGARTY: 25 Q So do you agree that the weaker the</p> | <p>1 makes the statement that: "Any conclusion" -- 2 make sure I read this right. 3 You say: "Any conclusion reached on 4 dose-response, uncontrolled confounding or 5 selection bias that relied upon or were influenced 6 by data analysis, opinions or conclusions 7 presented within these studies and report, are at 8 a high risk of bias." 9 Did I read that correctly? 10 A You did. 11 Q First identify any such conclusions that 12 relied on or were influenced by either the 2003 or 13 2007 papers or the 2009 submission. 14 A Again, I think we went through this 15 before. We know that these data were presented to 16 FDA, advocated to FDA at different times, so we 17 know that FDA reviewed these data. So I think 18 that certainly we can say FDA considered these 19 data as part of their decision-making. 20 Q That's not my question, Doctor. 21 My question is, identify any conclusions 22 that relied on or were influenced by either the 23 2003 or 2007 papers or the 2009 submission. 24 A Again, I would presume that FDA's 25 conclusions relied upon this data because they --</p> |

April Zambelli-Weiner, Ph.D.

| Page 403 | Page 405 |
|--|---|
| <p>1 they stated their intent to review it carefully, 2 they posted it to the docket. They obviously 3 considered this as part of their decision-making 4 process.</p> <p>5 Q Who at FDA relied on either of these 6 documents?</p> <p>7 A Again, I think we went through this 8 before, that I, you know, certainly can't pinpoint 9 who specifically did the review. You know, we can 10 talk about who was on the denial letter, but we 11 don't have a lot of detail about how FDA conducted 12 their review, who reviewed what, how much weight 13 they gave to things specifically. You know, we -- 14 we went through that before.</p> <p>15 Q What was the extension -- extent of 16 their reliance?</p> <p>17 A Again, I -- I have no personal knowledge 18 of exactly how much weight they gave to any pieces 19 of evidence. But again, you know, my supposition 20 based on -- it's my opinion that they did rely on 21 these data in a meaningful way based on the 22 language in their -- the language in their denial 23 letter. The fact that we don't see a lot of other 24 citations -- I mean, again presumably, FDA would 25 in making their decision-making publish and</p> | <p>1 regard to a safety issue with any product. 2 A I definitely have. I -- you know, I'm 3 not sure I can name names at the moment. But I -- 4 I absolutely have.</p> <p>5 Q Well, name a product. 6 A I can't -- I'm not sure I can name a 7 product either based on confidentiality. 8 Q Can you name a product without 9 confidentiality?</p> <p>10 A Well, I can name product categories. I 11 can talk about cardiac rhythm technologies. I can 12 talk about lung imaging technologies.</p> <p>13 Q Doctor -- 14 MR. TISI: She's trying -- she's not 15 finished.</p> <p>16 THE WITNESS: I'm trying to answer your 17 question.</p> <p>18 MR. HEGARTY: Well, she's not answering 19 my question.</p> <p>20 MR. TISI: Well, but you -- but you -- 21 but she said -- Counsel --</p> <p>22 BY MR. HEGARTY:</p> <p>23 Q If you're -- 24 MR. TISI: -- you asked her a question 25 about communications with the FDA under any</p> |
| <p>1 produce other pieces of -- of evidence that they 2 relied upon. So the prominence that this data has 3 on the docket, you know, and any other documents 4 leads me to believe that they did rely upon it.</p> <p>5 Q Well, why don't you cite for us your 6 extensive experience in dealing with FDA when 7 they're considering a Citizen Petition.</p> <p>8 A Again, I think I've been very honest 9 about my opinion about this and my experience with 10 this. I don't have any direct experience. I'm 11 basing it on my review of -- of the docket, of the 12 denial letter. That's --</p> <p>13 Q Cite for me all your experience in 14 communicating with FDA about any product.</p> <p>15 A Again, I am in the business of helping 16 clients submit data to FDA. So from that 17 perspective, I do have expertise. I understand 18 the kinds of things that FDA looks for. I don't 19 have any specific communication with FDA over a 20 Citizen Petition, if that's what you're asking me.</p> <p>21 Q You have never had any direct 22 communication with anyone at FDA ever, have you?</p> <p>23 A That is not accurate.</p> <p>24 Q Tell me when -- cite for me any instance 25 when you've had direct communication with FDA with</p> | <p>1 circumstances and you asked her categories, and 2 she's answering. You got to let her answer.</p> <p>3 BY MR. HEGARTY:</p> <p>4 Q If you're communicating with FDA, that 5 communication is not confidential or protected. 6 Is that what you're -- is that the position you're 7 taking?</p> <p>8 MR. TISI: Actually, that's not true, 9 Counsel, and you know that. In many instances 10 it's protected from -- from competitors. 11 Absolutely it is. Absolutely it is.</p> <p>12 MR. HEGARTY: I don't agree, and we're 13 not -- that's not --</p> <p>14 MR. TISI: Absolutely. Well --</p> <p>15 BY MR. HEGARTY:</p> <p>16 Q I'm just asking if that's your opinion.</p> <p>17 A My opinion is that any work that I do on 18 behalf of my clients working with -- with 19 regulatory agencies or with regulatory consultants 20 or in any capacity is -- is confidential, yes.</p> <p>21 Q You have never communicated with the FDA 22 about a Citizen Petition, correct?</p> <p>23 A I believe that is correct.</p> <p>24 Q You have no personal knowledge of 25 anything the FDA did with regard to evaluating the</p> |

April Zambelli-Weiner, Ph.D.

| Page 407 | Page 409 |
|--|---|
| <p>1 2008 and 1994 Citizen Petition, do you?</p> <p>2 A I believe I have answered that</p> <p>3 repeatedly, yes.</p> <p>4 Q And what is your opinion based on that</p> <p>5 you said -- where you said that they did rely on</p> <p>6 the 2003 and 2007 papers and the 2009 submission?</p> <p>7 A Again, I think I've already answered</p> <p>8 that repeatedly.</p> <p>9 Q It's only -- it's only what's in the</p> <p>10 2014 denial letter, correct?</p> <p>11 A That's not correct. I believe I cited</p> <p>12 the meeting that the PCP -- PCPC and J&J had with</p> <p>13 FDA, and the docket as well.</p> <p>14 Q And where do you cite those?</p> <p>15 A In here, in my report.</p> <p>16 Q Show me.</p> <p>17 A Let's see. (Peruses document.)</p> <p>18 So, in "Other documents considered,"</p> <p>19 number 1 is the e-mail from John Bailey regarding</p> <p>20 the meeting with FDA.</p> <p>21 And I believe the docket is -- is cited</p> <p>22 in here as well.</p> <p>23 Q Where is it cited?</p> <p>24 A You want me to look for it?</p> <p>25 Q Yes.</p> | <p>1 support an opinion that FDA was influenced by the</p> <p>2 2009 and -- response and the 2003 and 2007 papers?</p> <p>3 A Well, again, I think it supports -- it</p> <p>4 supports that they reviewed that and considered</p> <p>5 that as part of their decision-making.</p> <p>6 Q Okay. Can you list for me everything</p> <p>7 they reviewed and considered?</p> <p>8 A Again, we went -- we went through this</p> <p>9 before. But, no, because there's really a lack of</p> <p>10 detail in the denial letter about what their</p> <p>11 process was and -- and what specifically they</p> <p>12 reviewed.</p> <p>13 But, again, you know, in my opinion as</p> <p>14 an expert, I would have expected them to -- to</p> <p>15 provide detail on -- on the things that they</p> <p>16 reviewed, and they don't provide a lot of -- a lot</p> <p>17 of other documents, but they do specifically refer</p> <p>18 to -- refer to this, and this exists on the</p> <p>19 docket.</p> <p>20 Q How many responses to citizen petitions</p> <p>21 have you read?</p> <p>22 A I'm not certain.</p> <p>23 Q Can you cite for me any other response</p> <p>24 to a Citizen Petition you've read by FDA?</p> <p>25 A I believe I've read some around tobacco</p> |
| Page 408 | Page 410 |
| <p>1 A It's either in a footnote or it's cited.</p> <p>2 I'm trying to think of where. (Peruses document.)</p> <p>3 Q How much time do you need, Doctor?</p> <p>4 A I think it's -- I'm not certain, but</p> <p>5 I -- I think it's footnote 3 on page 8.</p> <p>6 MR. TISI: Correct.</p> <p>7 MR. HEGARTY: Are you saying "correct"</p> <p>8 for her?</p> <p>9 MR. TISI: What? I'm sorry.</p> <p>10 MR. HEGARTY: Did you say "correct"?</p> <p>11 MR. TISI: I -- I just answered the --</p> <p>12 I'm sorry.</p> <p>13 MR. HEGARTY: And when I said, Did you</p> <p>14 just say "correct," I was referring to counsel for</p> <p>15 the plaintiff.</p> <p>16 MR. TISI: No, she -- she said,</p> <p>17 "Correct." She said, "Correct."</p> <p>18 BY MR. HEGARTY:</p> <p>19 Q Where on page 3?</p> <p>20 A I'm sorry, I said page 8, footnote 3.</p> <p>21 Q Your -- your contention is that's where</p> <p>22 that cite is to?</p> <p>23 A I believe so.</p> <p>24 Q And how does being on -- being on the</p> <p>25 docketing statement in the letter from John Bailey</p> | <p>1 products.</p> <p>2 Q Okay. Cite for me one product.</p> <p>3 MR. TISI: Objection.</p> <p>4 THE WITNESS: I -- I can't recall</p> <p>5 specific products.</p> <p>6 BY MR. HEGARTY:</p> <p>7 Q If you would turn to page 6 -- I'm</p> <p>8 sorry, return to Exhibit 6.</p> <p>9 MR. HEGARTY: Would you hand her</p> <p>10 Exhibits 6 and 7, please.</p> <p>11 MR. TISI: I've got it here, 6. Here</p> <p>12 is 6. And I don't -- I don't see 7.</p> <p>13 BY MR. HEGARTY:</p> <p>14 Q First, as to page 6 --</p> <p>15 MR. TISI: I don't -- I don't have 7.</p> <p>16 I'm sorry. Hold on. Do you need both --</p> <p>17 MR. HEGARTY: Well, we'll start with</p> <p>18 page -- we'll start with Exhibit 6.</p> <p>19 BY MR. HEGARTY:</p> <p>20 Q First is Exhibit 6.</p> <p>21 Can you cite for me any other occasion</p> <p>22 when you've written to a journal who published an</p> <p>23 article asking for the procedure for reporting on</p> <p>24 concerns that you identified in that article?</p> <p>25 A I may have. I don't recall.</p> |

April Zambelli-Weiner, Ph.D.

| Page 411 | Page 413 |
|--|--|
| <p>1 Q You have never written a Letter to the 2 Editor identifying concerns that you have 3 identified with regard to any article, have you? 4 A Well, I'm recalling one, but I just want 5 to be accurate. I'm going to just flip to my CV 6 real fast. I want to make sure I accurately 7 characterize it. (Peruses document.) 8 So I'm just recalling the chondrolysis 9 article, and I -- I'm just not sure if it was a 10 Letter to the Editor or not. So... 11 Q And what page are you looking at? 12 A Page 58. 13 Q Which reference? 14 A The Hasan paper, the chondrolysis paper. 15 It's at the very top, it's the first one. 16 Q Do you think that's a Letter to the 17 Editor commenting on the -- on concerns you've had 18 with another article? 19 A I don't recall. I'm just saying I don't 20 recall the format of that article. It may be. 21 It's been a while. I'm trying to -- to recollect. 22 Q Other than that possible article, can 23 you cite for me any other occasion you've written 24 a Letter to the Editor criticizing or commenting 25 on what another author or authors wrote in a</p> | <p>1 Q Are there any plans to do it going 2 forward? 3 A There are plans to do it going forward. 4 Q When? 5 A I can't answer that. 6 Q Well, there's -- is there anything -- 7 any timetable set up? 8 A No, because I'm just doing it on my own 9 time, so it has to be worked in. 10 Q Also, with regard to Exhibit No. 7, 11 which is the one we can't find but I'll hand you 12 my copy, that's another correspondence that you 13 had with regard to either the 2003 or 2007 paper. 14 Has there been any further 15 correspondence with that journal since the last 16 dated e-mail there? 17 A No. I would say same answers. 18 Q You also mentioned earlier that when you 19 were asked if you were going to submit your report 20 to be peer reviewed, you said, "Not yet." 21 Do you have any plans to do that? 22 A Well, again, I think a lot of what's in 23 my report could potentially fall within the 24 purview of a Letter to the Editor, but I'm still 25 evaluating what format I'll -- I'll do that.</p> |
| <p>1 paper? 2 A Not that I can recall. 3 Q The last communication with the 4 publication listed in Exhibit No. 6 is dated 5 December 4, 2018. 6 Has there been any further communication 7 or activity with regard to this journal? 8 A I don't believe so. 9 Q Have you drafted a response to the 10 article, the 2000 -- first of all, does this 11 concern the 2003 or the 2007 article? 12 A Well, it would concern both, but I'm not 13 sure. This one looks like it's to the European 14 Journal of Cancer Prevention. 15 Q And that's the 2007 article? 16 A Right, but I think it's also the 2011 17 article, if I recall correctly. 18 Q Have you written or has anybody at your 19 office written a Letter to the Editor or other 20 proposed submission to either of these journals 21 with regard to the 2003 or 2007 papers? 22 A I have not done anything yet. I've 23 been -- been a little busy. 24 Q Has anybody in your office done that? 25 A No.</p> | <p>1 Q Well, have you written your report in a 2 different format? 3 A No, I haven't. 4 Q Have you -- do you have any timetable 5 for submitting your report in its current or a 6 different format? 7 A Not yet. 8 Q You reviewed for purposes of your report 9 three documents: The 2003, the 2007 articles, and 10 the 2009 response. Correct? 11 A Correct. 12 Q In those documents there are references 13 to multiple other articles including case-control 14 studies, correct? 15 A I would presume that would be correct. 16 Q Did you review any of those other 17 articles or any other articles with the same 18 critical eye that you reviewed the 2003 and 2007 19 articles or the 2009 response? 20 A Again, that wasn't my -- that wasn't my 21 task. That wasn't my charge to do, you know, a 22 broad evaluation of the entire evidence base. 23 So I think we talked about previously 24 that, you know, my focus was really a critical 25 appraisal of these studies that industry put</p> |

April Zambelli-Weiner, Ph.D.

| Page 415 | Page 417 |
|--|---|
| <p>1 forward to FDA, to the medical and scientific 2 community, around the causal or lack -- their 3 position of the lack of causal association between 4 talc and ovarian cancer. So that was my focus. 5 It was not a broader focus than that.</p> <p>6 Q Well, did any -- anything prevent you 7 from looking at the Cramer 1999 study and doing 8 the same thing with that study as you did with the 9 2003 Huncharek study?</p> <p>10 A Well, again, I mean certainly that could 11 be done, but that was not -- that was not my task, 12 that was not my charge.</p> <p>13 Q Did you ask to be able to do that?</p> <p>14 MR. TISI: Objection. Communications 15 with counsel.</p> <p>16 THE WITNESS: No.</p> <p>17 MR. TISI: I'm sorry. Communications 18 with counsel.</p> <p>19 BY MR. HEGARTY:</p> <p>20 Q Could you have done that?</p> <p>21 A Well, certainly that could be done as 22 part of a larger weight of evidence or a causation 23 analysis or, you know, any paper could be -- could 24 be critically reviewed, but this had a very 25 specific focus.</p> | <p>1 BY MR. HEGARTY: 2 Q Is that correct? 3 MR. TISI: Objection, Counsel. Improper 4 question. 5 MR. HEGARTY: No, it's not -- 6 MR. TISI: It is. She's -- 7 MR. HEGARTY: It's not improper. 8 MR. TISI: She's not here to -- to -- 9 BY MR. HEGARTY: 10 Q No, I'm going to put on the record, I'm 11 asking you to do the analysis -- same analysis you 12 did on the -- 13 MR. TISI: And I'm going to object as an 14 improper question. 15 BY MR. HEGARTY: 16 Q Well, if you say to me that I have the 17 ability to give it to you to do the analysis, I'm 18 going to give those studies to you and expect the 19 analysis. 20 MR. TISI: Well, and then I'm going to 21 ask you to have your experts be available to me so 22 that I can speak to them about an analysis that 23 they've done. Improper question. 24 You don't have to -- 25 MR. HEGARTY: My expert --</p> |
| <p>1 Page 416</p> <p>2 Q And that very specific focus was what 3 plaintiffs' counsel gave to you, correct? 4 A That's not how I characterized it. 5 Again, I characterized it as the key literature 6 that industry put forward to FDA, which is very 7 important to support very important points around 8 a causal analysis related to this question. 9 Q Well, you made reference in your report 10 to the Chang study. Did you go to the Chang study 11 and see if they did that study properly? 12 A Again, no. But had you put forward 13 Chang, I would have done the same review. 14 Q How long would that have taken? 15 A I don't know. 16 Q You referenced the Harlow study and said 17 they didn't talk about the Harlow study. Did you 18 do an analysis of the Harlow study to see if it 19 was valid and reliable? 20 A Again, same answer: Not my charge, not 21 my task. Had -- had industry put that forward as 22 their key evidence, I would have done the same 23 review as I did here. 24 Q So if I ask you to do those reviews, you 25 will do it? MR. TISI: Objection.</p> | <p>1 MR. TISI: You don't have to answer that 2 question. 3 MR. HEGARTY: My expert didn't offer to 4 do the analysis. 5 MR. TISI: You don't have to answer that 6 question because -- because you're not being 7 retained by Mr. -- Mr. Hegarty's client to do the 8 analysis that -- that he's asking you to do on the 9 spot here. 10 MR. HEGARTY: Let's go off the record. 11 I need to coordinate with transferring the -- the 12 witness for the remaining time. Off the record. 13 THE VIDEOGRAPHER: The time is 2:48 14 p.m., and we're going off the record. 15 (Recess.) 16 THE VIDEOGRAPHER: The time is 2:55 17 p.m., and we're back on the record. 18 DIRECT EXAMINATION 19 BY MR. KLATT: 20 Q Good afternoon, Doctor. My name is Mike 21 Klatt, and I represent Imerys Talc America in this 22 matter. 23 By your own testimony back on 24 January 11th, 2019 -- which was the first session 25 of the deposition, right?</p> |

April Zambelli-Weiner, Ph.D.

| Page 419 | Page 421 |
|---|---|
| <p>1 A Correct. 2 Q -- and today, you said you performed 3 what you described as a critical analysis of three 4 Huncharek or Muscat articles and one submission by 5 them to the FDA; is that correct? 6 A Correct. 7 Q Now, to date, as we sit here in February 8 2019, you'd agree with me that there's been well 9 over two dozen studies published, whether they're 10 prospective studies, retrospective studies, cohort 11 studies, case-control studies, meta-analyses, on 12 genital use of talc and ovarian cancer? 13 MR. TISI: Objection. 14 THE WITNESS: I would say that, first of 15 all, I wasn't tasked with a broader review of the 16 literature, so I -- I'm sure I can agree that 17 there's a broader literature out there, but I 18 can't speak to specifically what exists. 19 BY MR. KLATT: 20 Q Well, Doctor, you cite over 24 of those 21 studies in your report, in your references or 22 materials considered, right? 23 A Again, I'm going to rely on you for the 24 number, but certainly, you know, to the extent 25 that studies were cited within these articles,</p> | <p>1 done for the Huncharek and Muscat articles and 2 submission, correct? 3 A Well, I'm not sure about your -- your 4 terminology, but what I will agree to is that I 5 wasn't tasked with doing that, and therefore, 6 you're correct, I did not -- I did not do a 7 critical appraisal of the broader evidence base on 8 talc and ovarian cancer. 9 Q Now, have you or any of your employees 10 at TTi or anyone else acting at your direction 11 sent e-mails or otherwise communicated with the 12 editors of any of the journals that have published 13 these over two dozen studies relating to talc and 14 ovarian cancer? 15 A I'm sorry. Are you asking specifically 16 related to these studies? 17 Q Correct. 18 A Not to my knowledge. 19 Q In Exhibits 6 and 7, you communicated 20 with two journals specifically requesting 21 corrections or retractions of Huncharek and Muscat 22 articles on talc and ovarian cancer, correct? 23 A Well, again, I haven't looked at those 24 in a long time, so just to your language, I'm not 25 sure that we were calling for the retraction as</p> |
| <p style="text-align: center;">Page 420</p> <p>1 yes, that's correct. 2 Q I mean on page 46 through 50 of your 3 report, I can just read them out. Purdie, 1995; 4 Chang, 1997; Cramer, 1995; Green, 1997; Wong, 5 1999; Booth, 1989; Harlow, 1992; Cook, 1997; 6 Cramer, 1982; Harlow, 1989; Ness, 2000; 7 Rosenblatt, 1992; Whittemore, 1998; Chen, 1992; 8 Cramer, 1999; Gertig, 2000; Godard 1998; Tzonou, 9 1993; Hartge 1983; Gates, 2010; Gates, 2008; Gross 10 and Berg, 1995; Langseth, 2004; Langseth, 2008; 11 Mills, 2004; Terry, 2013. 12 These are all studies regarding talc and 13 ovarian cancer that you cited on pages 46 to 50 of 14 your report, correct? 15 A I -- I'm going to agree that, you know, 16 without looking at it, that you read that 17 correctly. I mean certainly again any studies 18 that relate to my analysis of these particular 19 articles, sure, would absolutely be in my work 20 cited. 21 Q And you said in response to 22 Mr. Hegarty's questions a short time ago that 23 you've not done the same sort of fly specking 24 critical analysis of any of these other papers or 25 studies of talc and ovarian cancer that you've</p> | <p style="text-align: center;">Page 422</p> <p>1 much as we were requesting the process, to 2 understand their process. 3 Q Doctor, I'm looking at Exhibit 6, and 4 the subject is "Re: Inquiry about European 5 Journal of Cancer Prevention Retraction." 6 And Exhibit 7, the e-mail is "Inquiry 7 About Retraction, Any Cancer Research Feedback 8 Form." Correct? 9 A Sorry, I'm trying to put my hands on -- 10 MR. HEGARTY: We have 6. We don't have 11 7. 12 MR. TISI: I thought you gave her your 13 copy of 7. 14 MR. HEGARTY: I gave that back to -- 15 here is Exhibit 7. He just put Exhibit 6 to your 16 left. 17 THE WITNESS: Thank you. 18 Right. So I think you read the title of 19 one of the e-mails, and then later in the e-mail, 20 you know, the body of the e-mail it says, you 21 know, what are -- what are the possible steps to 22 report these findings to the scientific community? 23 You know, is there a way to request a retraction? 24 Are there any other methods that you would 25 suggest?</p> |

April Zambelli-Weiner, Ph.D.

| Page 423 | Page 425 |
|--|---|
| <p>1 So my characterization of the e-mails 2 would be to inquire to the journals as to what 3 their process is for handling these kinds of 4 issues. 5 BY MR. KLATT: 6 Q And you've not attempted and no one 7 acting on your behalf has attempted in any way to 8 insert themselves, to tamper, monkey, meddle with 9 any of the other published literature on talc and 10 ovarian cancer other than these specific Huncharek 11 and Muscat articles, correct? 12 MR. TISI: Objection to your -- to your 13 question. 14 THE WITNESS: Again, I'm not agreeing 15 with your characterization of -- of the work that 16 I did. 17 But, again, my task was very focused on 18 these specific studies, and so I did not do that 19 broader analysis, nor would I have the basis at 20 this point in time to do that. So the answer to 21 your question is no. Again, not agreeing with 22 your characterization. 23 BY MR. KLATT: 24 Q You've had no other communication and no 25 one acting on your behalf has had any other</p> | <p>1 A So just to make sure I understand your 2 question, I assume you're asking that question 3 specifically related to those studies. 4 Q And the communications that you or those 5 acting at your direction have had with the editors 6 of the journals that have published the Huncharek 7 and/or Muscat articles. 8 MR. TISI: Objection. 9 THE WITNESS: I'm sorry, I lost that -- 10 I lost that line. 11 BY MR. KLATT: 12 Q Let me start over. 13 A Thank you. 14 Q You've communicated or people acting at 15 your behalf have communicated with the editors of 16 journals that have published Huncharek and/or 17 Muscat studies requesting the procedures to 18 request corrections or retractions of those 19 specific articles, correct? 20 A Correct. 21 Q Neither you nor anyone else acting at 22 your direction has had any communication with the 23 over two dozen other prospective cohort studies, 24 retrospective case-control studies or other 25 meta-analyses dealing with talc and ovarian cancer</p> |
| <p>1 communication with any of the editors of the 2 journals publishing the articles on talc and 3 ovarian cancer, whether prospective studies, 4 retrospective case-control studies or 5 meta-analyses, requesting any sort of retraction 6 or correction of any of those articles, right? 7 MR. TISI: Objection, other than these 8 two. 9 BY MR. KLATT: 10 Q Other than the two Huncharek and Muscat 11 articles that you have -- 12 MR. TISI: Well, there's actually four 13 Muscat and Huncharek articles. 14 BY MR. KLATT: 15 Q Other than the Huncharek and Muscat -- 16 THE VIDEOGRAPHER: Counsel, your 17 microphone fell off. 18 BY MR. KLATT: 19 Q Other than the three Huncharek and 20 Muscat articles and the submission, you and no one 21 acting on your behalf has attempted to contact any 22 of the editors of any of the journals that have 23 published the prospective cohort studies, the 24 retrospective case-control studies or the other 25 meta-analyses of talc and ovarian cancer, correct?</p> | <p>1 to request any sort of corrections or retractions 2 of those articles, right? 3 A That's correct. We -- we -- it feels 4 like the same question as before, but, yes, that's 5 correct. 6 MR. KLATT: Thank you. 7 MR. LOCKE: Let me -- oh, I was just 8 going to try to shoot between the two of you. But 9 thanks. Thanks. 10 DIRECT EXAMINATION 11 BY MR. LOCKE: 12 Q Doctor, my name is Tom Locke. I 13 represent the Personal Care Products Council. I 14 have relatively few questions for you. 15 A Okay. 16 Q Epidemiology is a field that takes years 17 of academic training to learn; is that correct? 18 A I would say that's true, yes. 19 Q How long did it take you to earn your 20 doctorate in epidemiology? 21 A Four years. 22 Q And you had a master's degree that was 23 related prior to that; is that correct? 24 A That's correct. 25 Q And you conducted postdoctoral</p> |

April Zambelli-Weiner, Ph.D.

| Page 427 | Page 429 |
|---|---|
| <p>1 epidemiology training after you obtained your 2 doctorate?</p> <p>3 A That's correct. I had a post-doc at 4 Johns Hopkins.</p> <p>5 Q Only a person with epidemiological 6 training would be able to determine an error -- an 7 epidemiologic error in an epidemiologic study; is 8 that correct?</p> <p>9 MR. TISI: Objection. Calls for 10 speculation.</p> <p>11 THE WITNESS: I don't know that I would 12 necessarily agree with that. I mean, I think 13 people have different levels of training and 14 different levels of experience working in the 15 field. So I think that's probably not exactly 16 true.</p> <p>17 BY MR. LOCKE:</p> <p>18 Q Well, when you say "working in the 19 field," let me just ask you -- well, let's break 20 it down.</p> <p>21 Could an ordinary high school graduate 22 read a study or paper like Dr. Huncharek and 23 Dr. Muscat's 2009 submission to the FDA and 24 identify the errors that you claim to have found?</p> <p>25 MR. TISI: Objection.</p> | <p>1 larger -- the concepts that you're talking about, 2 I think those are more epi -- epidemiological, 3 methodological -- sorry, it's been a long day -- 4 concepts.</p> <p>5 BY MR. LOCKE:</p> <p>6 Q So it takes someone with epidemiological 7 training to analyze a report or study like what 8 Drs. Huncharek and Muscat did in 2009 and identify 9 if there are problems with that study.</p> <p>10 MR. TISI: Objection.</p> <p>11 THE WITNESS: Again, I'm going to kind 12 of -- it's kind of an amorphous question, right? 13 I mean there's people with a lot of epidemiologic 14 training. There's people who practice 15 epidemiology who are clinicians who have learned 16 on the job. So your specific question was about 17 training, and I would say there's probably some 18 exceptions to that.</p> <p>19 BY MR. LOCKE:</p> <p>20 Q Well, people are going to have to 21 understand epidemiology pretty well in order to 22 identify the errors that you've identified; is 23 that correct?</p> <p>24 A I would say that's certainly true of 25 some of the errors, yes.</p> |
| Page 428 | Page 430 |
| <p>1 THE WITNESS: Well, I would say some of 2 them, probably yes. I would think probably just 3 about anyone could do like a crosscheck between 4 the data reported in the study and the data 5 reported in the original studies. So I think 6 certain errors, it's possible.</p> <p>7 BY MR. LOCKE:</p> <p>8 Q Are you talking about typographic 9 errors?</p> <p>10 A No, I was talking about the number of 11 errors, the abstraction errors.</p> <p>12 Q So in your opinion, it does not take an 13 expert in epidemiology to be able to look at 14 relative risks, ORs, all the other types of 15 terminology and -- to identify the errors that 16 exist -- that you contend exist in Dr. Huncharek 17 and Dr. Muscat's report?</p> <p>18 MR. TISI: Objection.</p> <p>19 THE WITNESS: Well, no, I don't think 20 that's exactly what I was saying. I think you 21 asked me could someone with a high school 22 education pick out any of the errors, and I was 23 simply pointing out that I think there's some of 24 the errors that they could probably identify.</p> <p>25 But, you know, with regard to the</p> | <p>1 Q Well, referring specifically to the 2 epidemiologic errors, is that true with respect to 3 the epidemiologic errors? I'm not talking about 4 typos or misspellings or those kinds of things.</p> <p>5 A I'm sorry, can you repeat your question 6 or rephrase?</p> <p>7 Q Sure.</p> <p>8 I'm asking you, you know, it's not a -- 9 you're going to have to have epidemiological 10 experience or training in order to identify the 11 types of epidemiologic errors that you contend are 12 contained in the 2009 submission drafted by 13 Drs. Huncharek and Muscat?</p> <p>14 A So I would agree with -- I -- I will 15 sort of agree with your statement because, again, 16 I'm thinking of the exceptions. You know, I have 17 people who work for me who have bachelor's 18 degrees, and they wouldn't necessarily have 19 specific training in epidemiology, but I sure am 20 impressed with what they're able to pick out from 21 these studies.</p> <p>22 So I'm just saying, you know, I might 23 generally agree with you, but I don't think that 24 holds true all of the time.</p> <p>25 Q And the people that work for you,</p> |

April Zambelli-Weiner, Ph.D.

| Page 431 | Page 433 |
|--|--|
| <p>1 they're working for a post -- a person with 2 postdoctorate training in epidemiology. That's 3 their job is to work in and on epidemiologic 4 matters, correct?</p> <p>5 A That is true, correct.</p> <p>6 Q Do you know whether PCPC in 2009 7 employed persons with epidemiological training 8 like yourself?</p> <p>9 A No, I couldn't say.</p> <p>10 Q Earlier today you stated that 11 Drs. Huncharek -- or that Dr. Huncharek and 12 Dr. Muscat's material was misleading. Let me just 13 stop there.</p> <p>14 Is that an accurate characterization of 15 what you had said about their work?</p> <p>16 A Yes, I think that there are aspects of 17 their -- of their reports that are misleading, 18 that's correct.</p> <p>19 Q Let me ask you -- but you also testified 20 that you had no idea what their intent was; is 21 that correct?</p> <p>22 A That's correct. I mean, I can't know, 23 you know, did they intend to mislead or was there 24 just, you know, not good quality control, massive 25 errors. I mean, I can't know what their intent</p> | <p>1 would say, no, because to me that gets to intent, 2 but I think that taking the facts of the 3 studies -- I'm definitely speaking to the facts as 4 they exist with regard to scientific standards.</p> <p>5 BY MR. LOCKE:</p> <p>6 Q Are you a medical ethicist?</p> <p>7 A No.</p> <p>8 Q Are you a scientific ethicist?</p> <p>9 A No, I wouldn't characterize myself that</p> <p>10 way.</p> <p>11 Q Are you a legal ethicist?</p> <p>12 A No.</p> <p>13 Q You're not offering an opinion regarding 14 whether a person or entity may submit materials to 15 the FDA; is that correct?</p> <p>16 MR. TISI: Objection.</p> <p>17 THE WITNESS: I'm not sure I understand 18 the question.</p> <p>19 BY MR. LOCKE:</p> <p>20 Q Well, are you offering an opinion 21 regarding whether it's appropriate for a person or 22 entity to submit materials to the FDA?</p> <p>23 A No, I'm not.</p> <p>24 Q When did you first work on talc and 25 ovarian cancer epidemiology issues in any</p> |
| <p>1 was. I can simply state what I'm able to discern 2 as -- as an expert reviewing -- reviewing these 3 papers.</p> <p>4 Q So would it be better to use the word -- 5 or strike that.</p> <p>6 Rather than using the word "misleading," 7 would it be more appropriate to state that 8 Dr. Huncharek and Dr. Muscat in your view made 9 errors?</p> <p>10 MR. TISI: Objection.</p> <p>11 THE WITNESS: Not -- not necessarily. I 12 think they did make errors. I think that's 13 obvious. I think that their data is misleading. 14 I think that, you know, there are decisions that 15 are made, again for whatever reason, to 16 characterize a particular study in a particular 17 way that is misleading or inaccurate. So I think 18 those are both true. I would -- I would stick 19 with both of those.</p> <p>20 BY MR. LOCKE:</p> <p>21 Q Are you offering an opinion that 22 Dr. Huncharek and Dr. Muscat acted in an unethical 23 manner?</p> <p>24 MR. TISI: Objection.</p> <p>25 THE WITNESS: I think again I'm -- I</p> | <p>1 capacity?</p> <p>2 A I think I previously stated that I can't 3 be certain that I never read any of these papers 4 before, just having worked in the area of cancer 5 for a good bit of my career. So I really can't 6 pinpoint that time. If you're asking me a more 7 specific question around my engagement, I'll try 8 to answer that to the best of my ability.</p> <p>9 Q Well, let me ask you a more specific 10 question.</p> <p>11 When did you first begin analyzing 12 Dr. Huncharek and Dr. Muscat's materials on talc/ 13 ovarian cancer epidemiology?</p> <p>14 A Hmm. I -- I don't recall specifically.</p> <p>15 Q Well, was it before or after you were 16 contacted by any of plaintiffs' counsel in this 17 litigation?</p> <p>18 A In any capacity?</p> <p>19 Q In any capacity.</p> <p>20 A I would say it was after.</p> <p>21 MR. TISI: I think we're done.</p> <p>22 THE WITNESS: Again, to the best of my 23 recollection.</p> <p>24 MR. LOCKE: No, I don't think we're 25 done. I don't think we've hit our time.</p> |

April Zambelli-Weiner, Ph.D.

| Page 435 | Page 437 |
|---|---|
| <p>1 MR. TISI: I think you have. 2 How much time is left? 3 THE VIDEOGRAPHER: 18 minutes and 52 4 seconds. 5 MR. TISI: So you're a minute over, but 6 if you have a last question, I will -- 7 MR. LOCKE: Sure. 8 BY MR. LOCKE: 9 Q When was the first time you began 10 working as a testifying expert on talc and ovarian 11 cancer issues? 12 A I don't recall. I would rely on a 13 letter agreement or invoices to -- to verify that 14 because I'm just not sure. 15 Q Well, I want to get this cleared up. 16 MR. TISI: No, we're done. 17 MR. LOCKE: No, I -- 18 MR. TISI: No, we're done. 19 MR. LOCKE: Well, put it on the record 20 because I want to be crystal clear that you're 21 cutting me off and I can't follow up with this 22 last question. 23 MR. TISI: You're a couple of minutes -- 24 couple of minutes over. I've given you some 25 latitude here, Tom.</p> | <p>1 answer that. 2 MR. TISI: Yeah, you may be infringing 3 on -- to the extent that she's been consulting 4 with us. So it's a different -- it may be a 5 different question. 6 MR. LOCKE: Well, no, what I'm trying to 7 find out was, was there a period of time when she 8 was a consulting expert and then became a 9 testifying expert. 10 MR. TISI: You can ask her that 11 question. 12 BY MR. LOCKE: 13 Q Was there a period of time when you were 14 a consulting expert before you became a testifying 15 expert? 16 A Yes. 17 MR. TISI: No more questions. We're 18 done. I do have like two questions. 19 THE VIDEOGRAPHER: Counsel, your 20 microphone. 21 MR. TISI: Okay. 22 Let's go off the record. I just want 23 to -- 24 THE VIDEOGRAPHER: The time is 25 3:15 p.m., and we are going off the record.</p> |
| Page 436 | Page 438 |
| <p>1 MR. LOCKE: Okay. 2 MR. TISI: It's your job to divide -- 3 divide it up amongst yourselves -- 4 MR. LOCKE: Okay. 5 MR. TISI: -- and if you find yourself 6 without time, it's not my problem. 7 MR. LOCKE: Well, it actually is, but I 8 might -- we might go to the judge about it. Let's 9 just -- 10 MR. TISI: If you -- if you -- how 11 much -- how many more questions do you think you 12 have on this area? 13 MR. LOCKE: Well, it kind of depends on 14 the answer, but basically what I'm trying to find 15 out is was there -- 16 MR. TISI: Tom, I am going to -- 17 MR. LOCKE: One more question. 18 MR. TISI: One more question. Then -- 19 then have at it. 20 BY MR. LOCKE: 21 Q Was there a period of time between when 22 you became a testifying expert and when you -- 23 before which you were working on Dr. Huncharek and 24 Muscat's -- or analyzing their materials? 25 A Am I -- I'm not sure I'm allowed to</p> | <p>1 (Recess.) 2 THE VIDEOGRAPHER: The time is 3 3:19 p.m., and we are back on the record. 4 CROSS-EXAMINATION 5 BY MR. TISI: 6 Q Doctor, I just want to ask you just a 7 very brief couple of questions. 8 First of all, you were asked in the 9 first part of your deposition whether or not there 10 was information that you wanted and that you 11 requested that you did not have. 12 Do you remember that question? 13 A Correct. Yes, I do. 14 Q Okay. Would you turn to your report, 15 footnote 4 on page 9. 16 A Okay. 17 Q I'm going to read it into the record. 18 It says: "I requested additional documents 19 relating to the 2003 and 2007 studies by Huncharek 20 and Muscat that might have been in the possession 21 of Dr. Huncharek, who I understood did the primary 22 analysis. I was informed that Dr. Huncharek has 23 not been made available for deposition, and that 24 he claims the documents relating to his work on 25 talc were destroyed by a fire."</p> |

April Zambelli-Weiner, Ph.D.

| Page 439 | Page 441 |
|--|---|
| <p>1 Do you -- do you see that?</p> <p>2 A Yes.</p> <p>3 Q Okay. Why would it have been helpful to</p> <p>4 you to see the background documents, including</p> <p>5 drafts and communications and analyses, that would</p> <p>6 have been in the possession on the 2003, 2007, and</p> <p>7 for that matter, the 2009 and 2011 report and --</p> <p>8 and study?</p> <p>9 MR. HEGARTY: Objection. Form.</p> <p>10 THE WITNESS: Sure. I think I testified</p> <p>11 earlier today to the fact that there's a paucity</p> <p>12 in the methods, a lack of transparency, a lack of</p> <p>13 clarity in terms of what was done, and certainly,</p> <p>14 you know, any data that might have shed some --</p> <p>15 some light on that would have been very helpful in</p> <p>16 trying to evaluate the studies.</p> <p>17 BY MR. TISI:</p> <p>18 Q And have you been made aware that the</p> <p>19 plaintiffs' steering committee has attempted to</p> <p>20 subpoena Dr. -- Dr. Huncharek, and that the court</p> <p>21 actually ordered his deposition to -- to occur</p> <p>22 and -- or his documents to be produced, and that</p> <p>23 he has not made himself available?</p> <p>24 MR. HEGARTY: Objection. Form.</p> <p>25 THE WITNESS: Yes, I've been made aware</p> | <p>1 Q Do you see that?</p> <p>2 A Yes.</p> <p>3 Q Would you read the first sentence into</p> <p>4 the record, please.</p> <p>5 A Sure. "The results of this study appear</p> <p>6 to support the contention that talc exposure</p> <p>7 increases risk of ovarian carcinoma."</p> <p>8 Q Did Dr. Huncharek and Muscat, did they</p> <p>9 communicate that to the FDA, if you can recall?</p> <p>10 MR. HEGARTY: Objection. Form.</p> <p>11 THE WITNESS: Not that I recall.</p> <p>12 MR. TISI: No further questions.</p> <p>13 MR. HEGARTY: Can we go off the record</p> <p>14 for a second.</p> <p>15 THE VIDEOGRAPHER: The time is 3:23 p.m.</p> <p>16 We're going off the record.</p> <p>17 (Pause in the proceedings.)</p> <p>18 THE VIDEOGRAPHER: The time is 3:25 p.m.</p> <p>19 We're back on the record.</p> <p>20 (Exhibit No. 24 was marked for</p> <p>21 identification.)</p> <p>22 REDIRECT EXAMINATION</p> <p>23 BY MR. HEGARTY:</p> <p>24 Q Doctor, for purposes of the record, I've</p> <p>25 marked as Exhibit 24 the binder you brought of</p> |
| <p style="text-align: center;">Page 440</p> <p>1 of that.</p> <p>2 BY MR. TISI:</p> <p>3 Q The second question, you were referred</p> <p>4 to -- by Mr. Hegarty to Exhibit No. 22, the Chang</p> <p>5 article. Would you pull that up, please.</p> <p>6 A Sure.</p> <p>7 Q And I'm specifically going to turn your</p> <p>8 attention to page 2400.</p> <p>9 A I'm sorry. Chang. Okay.</p> <p>10 Q And this is a case-control study, 1997,</p> <p>11 correct?</p> <p>12 A That's correct.</p> <p>13 Q And this would have been -- this is one</p> <p>14 of the studies that Dr. Huncharek and Muscat told</p> <p>15 the FDA was part of the dataset that did not</p> <p>16 support a causal inference?</p> <p>17 MR. HEGARTY: Objection. Form.</p> <p>18 THE WITNESS: I believe that's correct.</p> <p>19 BY MR. TISI:</p> <p>20 Q Okay. Could you turn to the page 2400,</p> <p>21 the last paragraph, the concluding paragraph, and</p> <p>22 read the first sentence into the record, please.</p> <p>23 A Is it the one that starts "Differences"?</p> <p>24 Q No, it says "The results of this study."</p> <p>25 A Oh, sorry. Okay.</p> | <p style="text-align: center;">Page 442</p> <p>1 studies with you today; is that correct?</p> <p>2 A Correct.</p> <p>3 Q In talking about the 2009 response to</p> <p>4 the Citizen Petition, you have testified in the</p> <p>5 past that it is always appropriate to challenge</p> <p>6 the opinions of others, and this is the foundation</p> <p>7 of science. Correct?</p> <p>8 A Well, I'm not certain about the</p> <p>9 testimony. Certainly I don't recall all of my</p> <p>10 testimony, so I guess my answer would be I don't</p> <p>11 recall.</p> <p>12 Q Well, do you agree that it's always</p> <p>13 appropriate to challenge the opinions of others,</p> <p>14 and this is a foundation of science?</p> <p>15 A I think that I could agree that</p> <p>16 scientific debate is part of science and the</p> <p>17 scientific process.</p> <p>18 Q You were asked questions about being</p> <p>19 informed with regard to Dr. Huncharek's status.</p> <p>20 Who informed you of his status?</p> <p>21 A Plaintiff lawyers.</p> <p>22 Q And what additional documents did you</p> <p>23 request? You said, "I requested additional</p> <p>24 documents." What additional documents did you</p> <p>25 request?</p> |

April Zambelli-Weiner, Ph.D.

| Page 443 | Page 445 |
|--|--|
| <p>1 A Any, you know, analyses, protocols, any 2 supporting documentation related to the studies. 3 Q Did you report to FDA any problems that 4 you have had -- that you -- strike that. 5 Did you report to FDA the problems you 6 noted with regard to the 2009 response to the 7 Citizen Petition? 8 A No, I have not. 9 MR. HEGARTY: I'm going to mark as 10 Exhibit 25 the Langseth study. 11 (Exhibit No. 25 was marked for 12 identification.) 13 BY MR. HEGARTY: 14 Q You did review that study, did you not? 15 A Yes, I believe so at some point. 16 Q Can you turn over to the -- turn to the 17 last -- turn to page -- second page under the 18 "Proposal to Research Community." Do you see 19 that? 20 A Yes. 21 Q First of all, this is a meta-analysis, 22 correct? 23 A That's correct. 24 Q And it includes the forest plot that you 25 thought you would expect from the Huncharek study?</p> | <p>1 MR. TISI: Objection. 2 THE WITNESS: Again, not recalling their 3 specific language, they state the current body of 4 experimental and epidemiologic evidence, so 5 they're talking about a broader evidence base. 6 That's my interpretation of that particular 7 comment, but then having not read the paper 8 recently and having the full context. 9 BY MR. HEGARTY: 10 Q When you read the Langseth paper, did 11 you take issue with anything in it? 12 A Again, I wasn't charged with doing a 13 critical review of this paper, so it wasn't -- 14 wasn't the same task. 15 MR. HEGARTY: And that's probably -- is 16 that my time? 17 MR. TISI: He's done, although I have a 18 follow-up question to that, so I might as well 19 ask. 20 MR. HEGARTY: Okay. Was that my three 21 and a half, whatever? 22 THE VIDEOGRAPHER: 3 minutes and 29 23 seconds. 24 MR. HEGARTY: Okay. All right. Thank 25 you.</p> |
| <p style="text-align: center;">Page 444</p> <p>1 A That's correct. 2 Q And under the Proposal to Research 3 Community, the authors say: "The current body of 4 experimental and epidemiologic evidence is 5 insufficient to establish a causal association 6 between perineal use of talc and ovarian cancer 7 risk." 8 Did I read that correctly? 9 A You did read that correctly. 10 Q How is that a different conclusion than 11 what Drs. Huncharek and his other authors reached 12 in the 2003 meta-analysis? 13 MR. TISI: Objection. 14 THE WITNESS: Well, I think that's what 15 I was trying to describe earlier. This sounds 16 like they're making an assessment of the body of 17 literature at large. I haven't reread this paper. 18 My point earlier was it's inappropriate to infer 19 causation solely from the meta-analysis. 20 BY MR. HEGARTY: 21 Q How is this conclusion different than 22 what the 2009 response to FDA says -- I'm sorry, 23 the -- how is this different than the 2009 24 response that Drs. Huncharek and Muscat provided 25 to the FDA?</p> | <p style="text-align: center;">Page 446</p> <p>1 RECROSS-EXAMINATION 2 BY MR. TISI: 3 Q Doctor, I'd like to ask you two things 4 since counsel brought up the Langseth paper. 5 Could you please go to the "What this 6 study adds" section, the gray box in the very end, 7 and read the two bullet points, please. 8 First of all, you've seen these kinds of 9 boxes before -- 10 A Yes. 11 Q -- in these studies? 12 Why do they put them there? 13 MR. HEGARTY: Objection. Form. 14 THE WITNESS: They're emphasis just to 15 help people translate and distill the information 16 in the article. 17 BY MR. TISI: 18 Q Okay. Could you please identify -- read 19 the two bullet points into the record, please. 20 A Sure. "Epidemiological evidence 21 suggests that use of cosmetic talc in the perineal 22 area may be associated with ovarian cancer risk. 23 The IARC has classified this use of talc as 24 possibly carcinogenic to human beings," in 25 parentheses, "Group 2B."</p> |

April Zambelli-Weiner, Ph.D.

| Page 447 | Page 449 |
|--|--|
| <p>1 "The mechanism of carcinogenicity may be 2 related to inflammation. This paper focused on 3 the high degree of consistently in the studies 4 accomplished so far and what should be the focus 5 in future studies."</p> <p>6 Q And this was -- what was the date of 7 this article?</p> <p>8 A It looks like 2007.</p> <p>9 Q Okay. And this was one of the articles 10 that was put forth by Dr. Huncharek and Muscat?</p> <p>11 A That's correct, they do -- they do 12 discuss this paper.</p> <p>13 Q Did they -- did they tell the FDA that 14 the study suggested the use of cosmetic talc in 15 the perineal area may be associated with ovarian 16 cancer risk?</p> <p>17 MR. HEGARTY: Objection. Form.</p> <p>18 THE WITNESS: No. In fact, this is an 19 example of one of the data points they 20 mischaracterized and misrepresent.</p> <p>21 BY MR. TISI:</p> <p>22 Q One more question.</p> <p>23 MR. HEGARTY: Objection. Form.</p> <p>24 BY MR. TISI:</p> <p>25 Q Go to the abstract in the very front of</p> | <p>1 3:33 p.m., and we're back on the record.</p> <p>2 RECROSS-EXAMINATION</p> <p>3 BY MR. KLATT:</p> <p>4 Q Doctor, I'm asking you about the 5 Langseth article that Mr. Tisi just asked you 6 about.</p> <p>7 Do you see on the first page the four 8 authors' names: H. Langseth, S. Hankinson, 9 J. Siemiatycki, and E. Weiderpass?</p> <p>10 A Yes, I do.</p> <p>11 Q If you turn to the last page of the 12 article down under "Acknowledgments," do you see 13 the acknowledgements say: "The work reported in 14 this paper was initiated while SH," Sue Hankinson, 15 "JS," Jack Siemiatycki, "and EW," Elaine 16 Weiderpass, "were part of an IARC monographs 17 working group of the International Agency for 18 Research on Cancer"?</p> <p>19 Were you aware of that?</p> <p>20 A I don't recall that specifically.</p> <p>21 Q So in 2008, in this meta-analysis, they 22 said: "The epidemiologic evidence suggests the 23 use of cosmetic talc in the perineal area may be 24 associated with ovarian cancer risk."</p> <p>25 Correct?</p> |
| Page 448 | Page 450 |
| <p>1 the paper, and do you see the -- could you please 2 read the second to last -- excuse me, the last 3 sentence of the abstract, please.</p> <p>4 A Beginning "Some"?</p> <p>5 Q Yes, please.</p> <p>6 A "Some environmental exposures, notably 7 talc and asbestos, have been suspected as ovarian 8 carcinogens."</p> <p>9 Q Having read Dr. Muscat and Huncharek's 10 statement to the FDA, what, if anything, did they 11 tell the FDA about the presence of asbestos in 12 talc?</p> <p>13 MR. HEGARTY: Objection. Form.</p> <p>14 THE WITNESS: My recollection is that 15 they repeatedly assert that talc has been free of 16 asbestos for a very long time.</p> <p>17 MR. TISI: Thank you very much.</p> <p>18 MR. HEGARTY: Off the record for a 19 second.</p> <p>20 MR. TISI: Do you want to ask a 21 follow-up with our two minutes?</p> <p>22 THE VIDEOGRAPHER: The time is 3:31 p.m. 23 We're going off the record. 24 (A discussion was held off the record.) 25 THE VIDEOGRAPHER: The time is</p> | <p>1 A Correct, that's what it says.</p> <p>2 Q They don't say "causes," correct?</p> <p>3 A In that statement -- in that sentence, 4 that's correct, they don't say "cause."</p> <p>5 Q And in contrast, instead of saying 6 "suggests" or "may be," back over on the second 7 page of the article, "These IARC epidemiologists 8 say the current body of experimental and 9 epidemiologic evidence is insufficient to 10 establish a causal association." Correct?</p> <p>11 A You did read that correctly.</p> <p>12 Q And that's in 2008, correct?</p> <p>13 A I think it's 2007.</p> <p>14 Q 2007.</p> <p>15 And the FDA's perfectly capable of 16 reading this paper from start to finish 17 themselves, correct?</p> <p>18 MR. TISI: Objection.</p> <p>19 THE WITNESS: I would hope so.</p> <p>20 MR. KLATT: Thank you.</p> <p>21 MR. TISI: We're done.</p> <p>22 THE VIDEOGRAPHER: The time is 3:35 23 p.m., February 7, 2019.</p> <p>24 Going off the record, concluding the 25 videotaped deposition.</p> |

April Zambelli-Weiner, Ph.D.

| | |
|---|--|
| <p>1 (Whereupon, the deposition 2 of APRIL ZAMBELLI-WEINER, Ph.D. 3 was concluded at 3:35 p.m.) 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25</p> | <p>1 INSTRUCTIONS TO WITNESS 2 Please read your deposition over carefully and 3 make any necessary corrections. You should state 4 the reason in the appropriate space on the errata 5 sheet for any corrections that are made. 6 After doing so, please sign the errata sheet 7 and date it. 8 You are signing same subject to the changes 9 you have noted on the errata sheet, which will be 10 attached to your deposition. It is imperative 11 that you return the original errata sheet to the 12 depoing attorney within thirty (30) days of 13 receipt of the deposition transcript by you. If 14 you fail to do so, the deposition transcript may 15 be deemed to be accurate and may be used in court. 16 17 18 19 20 21 22 23 24 25</p> |
| <p>Page 452</p> <p>1 CERTIFICATE OF CERTIFIED SHORTHAND REPORTER 2 The undersigned Certified Shorthand Reporter 3 does hereby certify: 4 That the foregoing proceeding was taken before 5 me at the time and place therein set forth, at 6 which time the witness was duly sworn; That the 7 testimony of the witness and all objections made 8 at the time of the examination were recorded 9 stenographically by me and were thereafter 10 transcribed, said transcript being a true and 11 correct copy of my shorthand notes thereof; That 12 the dismantling of the original transcript will 13 void the reporter's certificate. 14 In witness thereof, I have subscribed my name 15 this date: February 10, 2019.</p> <p>16 _____ 17 _____ 18 LESLIE A. TODD, CSR, RPR 19 Certificate No. 5129 20 _____ 21 (The foregoing certification of 22 this transcript does not apply to any 23 reproduction of the same by any means, 24 unless under the direct control and/or 25 supervision of the certifying reporter.)</p> | <p>Page 454</p> <p>1 ----- 2 E R R A T A 3 ----- 4 PAGE LINE CHANGE 5 _____ 6 REASON: _____ 7 _____ 8 REASON: _____ 9 _____ 10 REASON: _____ 11 _____ 12 REASON: _____ 13 _____ 14 REASON: _____ 15 _____ 16 REASON: _____ 17 _____ 18 REASON: _____ 19 _____ 20 REASON: _____ 21 _____ 22 REASON: _____ 23 _____ 24 REASON: _____ 25</p> |

62 (Pages 451 to 454)

Golkow Litigation Services - 1.877.370.DEPS

April Zambelli-Weiner, Ph.D.

Page 455

1 ACKNOWLEDGMENT OF DEPONENT
2 I, _____, do hereby
3 certify that I have read the foregoing pages, and
4 that the same is a correct transcription of the
5 answers given by me to the questions therein
6 propounded, except for the corrections or changes
7 in form or substance, if any, noted in the
8 attached Errata Sheet.
9
10 _____

11 APRIL ZAMBELLI-WEINER, Ph.D. DATE
12
13

14 Subscribed and sworn to
15 before me this
16 _____ day of _____, 20 _____.
17 My commission expires: _____
18 _____

19 Notary Public
20
21
22
23
24
25